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Hydrocephalus, and Hydrocephalus with Meningocele: Their Treatment by Choroid Plexectomy—*by Dr. Leo M. Davidoff, Professor of Clinical Neurological Surgery, College of Physicians and Surgeons, Columbia University.*

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CARDIOVASCULAR SYSTEM AS THE EFFECTOR ORGAN IN PSYCHOSOMATIC PHENOMENA

GEORGE BURCH, M.D.
and
THORPE RAY, M.D.
New Orleans

Bodily functions have been known for many years to be disturbed by emotional stress. These physiologic disturbances may be manifested as symptoms referable to any organ system; e. g., the gastrointestinal tract, the genitourinary tract and the respiratory and cardiovascular systems. For unknown reasons there is a tendency for one system to predominate in its disturbances. Many isolated observations of these reactions have been described. Beaumont [1] described interesting observations concerned with formation of gastric juice. Although most of Pavlov's studies were concerned with conditional reflexes, many were related to disturbed psychic states. Cannon [2] conducted objective studies of gastrointestinal disturbances produced by psychic changes. Wolff and Wolf and their associates [3] observed directly the effect of psychic disturbances on the vascularity of the mucosa of the stomach and changes in secretion in the stomach and duodenum associated with emotional upsets. The effect of emotional stress on respiration has been shown to produce a different spirographic respiratory pattern from that of the normal relaxed subject.[4] Sighing respiration is commonly observed during periods of emotional stress, and its importance in diagnosis has been previously emphasized.[5] Increased depth of respiration has been demonstrated during unpleasant thoughts.[6] Respiratory disturbances may be reflected in the cardiovascular system because of close physiologic relationships; e. g., the pronounced vasoconstriction following deep inspiration [7] or the influence of respiration on venous return. These indicate the complicated integrations of psychosomatic dysfunctions among organ systems.

The extreme susceptibility of the cardiovascular system to psychic disturbances is particularly well known. Every one is familiar with the development of tachycardia following emotional experiences, hypertension, pallor of the skin and syncope with fear angina pectoris with excitement and hypertension with prolonged anxiety. In fact, the cardiovascular system has been claimed to be "the most frequent seat of vegetative manifestation of neurosis." [8] Symptoms referable to the heart occur in almost all neuroses.[5b] The temporary cardiovascular reactions of blushing, sweating, paling, changes in temperature, and so forth, are better known than the more subtle and often sustained reactions to prolonged emotional stress. Studies on the cardiovascular output during periods of emotional stress reflect the effect of the central nervous system on the cardiovascular system. Anxiety causes a considerable increase in cardiac output.[9] The increase in cardiac output is out of proportion to the consumption of oxygen [10] and may be independent of changes in blood pressure. Studies of Hickam and Cargill [9b] revealed an increase in cardiac output in medical students before examinations of 50 per cent over the "composed" level. The greatest increase was 180 per cent. Anxious patients show an increase during the resting state. Recalling unpleasant life situations has been shown to produce changes in blood pressure, cardiac output and respiration which were as great as those produced by exercise. Anger, fear, resentment,

From the Department of Medicine, Tulane University School of Medicine, and the Charity Hospital, New Orleans.

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9. (*a*) Wolf and Wolff.[3c] (*b*) Hickam, J. B., and Cargill, W. H.: Effect of Anxiety on the Cardiac Output, paper read at meeting of American Society for Clinical Investigation, 1947. (*c*) Stead, E. A., Jr.; Warren, J. V.; Merrill, A. J., and Brannon, E. S.: The Cardiac Output in Male Subjects as Measured by the Technique of Right Atrial Catheterization: Normal Values with Observations on the Effect of Anxiety and Tilting, J. Clin. Investigation **24**: 326, 1945. (*d*) Grollman, A.: The Cardiac Output of Man in Health and Disease, Springfield, Ill., Charles C Thomas, Publisher, 1932.

10. Wolf and Wolff.[3c] Stead, Warren, Merrill and Brannon.[9c]

frustration and depression produced a greater cardiac output, which remained elevated for a longer period of time than the usual response to a standard exercise test.[5c] Under emotional stress the efficiency of the cardiovascular system is definitely impaired; therefore sustained emotional stress is a burden on the cardiovascular system. Psychic trauma may act as the precipitating cause of heart failure.[11]

The occurrence of angina pectoris and then sudden cardiac death as a response to intense emotional stimuli is well known. A person may acquire a conditioned response to a life situation so that its reappearance or mere recollection results in angina pectoris. Furthermore, auricular fibrillation or flutter, premature contractions and paroxysmal tachycardia are frequent cardiac manifestations of anxiety states.[12] Palpitation dyspnea and precordial discomfort are among the most common cardiac complaints in psychic disturbances. The importance of neurocirculatory asthma in the Civil War, in World War I and to a lesser extent in World War II,[12a] is generally recognized. The electrocardiogram has been found[13] to change during psychic disturbances. These records are interesting and definite objective data indicating cardiac disturbances manifested particularly by change in the order of repolarization.

It is evident from the foregoing discussion that the somatic responses to psychic phenomena are well recognized. There are, however, several problems which deserve consideration. 1. Since psychic disturbances produce profound somatic reactions, often resulting in serious organic changes or even sudden death, the physician should routinely devote considerable attention to this problem in the proper management of his patient regardless of the disease state. 2. The existence of sustained anxiety states with prolonged somatic dysfunction with superimposed temporary but explosive psychic stress will result in serious organic disease. The importance and mechanisms of these phenomena are not well understood. There is a need to study these reactions in all organ systems. This is particularly important in the cardiovascular system, since its failure is the most common cause of death in man today, and it is becoming even more important as the life span increases. 3. The psychiatrist and psychologist are in great need of objective methods for approaching the problem of evaluating the mental processes. Because of the great reactivity of the cardiovascular system and especially the peripheral blood vessels to thought processes, the cardiovascular system is a good effector organ of psychic phenomena in both health and disease. In the past the approach has been mainly through the history and physical examination, and to a lesser extent through thermometric, electrocardiographic and ballistocardiographic and other studies on cardiac output. Some of these methods are cumbersome, impractical and often not informative. The extreme sensitivity and operative simplicity of the plethysmograph open a new approach to an understanding of the more subtle reactions. The accessibility and sensitivity of the vessels of the tips of the digits make such an approach practical, quantitative and objective. Reactions may be quantitated as to duration as well as degree. It is the purpose of this report to present studies of case histories and by use of a sensitive plethysmograph to demonstrate the potential as well as present value of plethysmography in man.

REPORTS OF CASES

The clinical data on 4 patients are presented first to illustrate certain facts related to psychosomatic phenomena concerning the cardiovascular system. Such problems as these are encountered frequently by all physicians.

Case 1.—J. C., a white man aged 44, entered the hospital complaining of a squeezing type of precordial pain which radiated into the left side of his neck and into the ulnar aspect of the left arm. The pain was not precipitated by exercise but occurred after a period of emotional excitement, particularly anger. The psychic disturbances resulting from worry about his ill wife and the problem of meeting the demands of his friends for new automobiles increased the ease with which the pain was produced. His family physician told him that he had angina pectoris. This was accepted fatalistically, thereby increasing his anxiety state and the episodes of pain. The entire physical examination and laboratory studies except the electrocardiogram (fig. 1) failed to reveal any abnormalities. He

Fig. 1.—Electrocardiogram on patient 1 during an episode of anginal pain precipitated by anxiety (*A*) and after recovery (*B*). During the pain there was depression of the S-T segments and T waves in leads I and V_2 to V_6, being particularly pronounced in leads V_2, V_3, V_4 and V_5. After recovery from the pain the S-T segments returned to normal.

appeared apprehensive and rather anxious about his cardiac state. When he entered the heart station to record the electrocardiogram the extreme concern and anticipation of the nature of the results produced a typical anginal pain which lasted about ten minutes. The electrocardiogram (fig. 1*A*) recorded during the period of pain showed changes in the S-T segment and the T wave, greatest in the V leads, typical of those observed in angina pectoris. Immediately after the pain disappeared another electrocardiogram was obtained which showed a reversion of the S-T segments and T waves to normal (fig. 1*B*). The patient was then given an appointment to report to the laboratory for a plethysmographic study. The patient immediately began to experience some concern about the study. When dressing to come to the laboratory he became restless, irritable and anxious. He experienced episodes of mild anginal pain. By the time he entered the laboratory he was so disturbed psychically that he began to perspire freely and to show pallor and apprehension. He removed all of his clothing except his shorts and was allowed to remain alone. The

11. Sodeman, W. A., and Burch, G. E.: Precipitating Causes of Congestive Heart Failure, Am. Heart J. **15**: 22, 1938.

12. Friedman, M.: Studies Concerning Etiology and Pathogenesis of Neurocirculatory Asthenia: III. Cardiovascular Manifestations of Neurocirculatory Asthenia, Am. Heart J. **30**: 478, 1945.

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observers were soon called back because the patient rushed into the hall suffering from a severe attack of angina pectoris associated with a syncopal syndrome. An electrocardiogram recorded during the pain revealed the changes in the S-T segment and the T wave previously observed which are typical of those encountered in angina pectoris. Glyceryl trinitrate (his first experience) relieved the pain, and another electrocardiogram recorded after the pain had fully disappeared was normal. The electrocardiographic changes were similar to those noted previously (fig. 1).

The relationship of the psychic disturbances to the episodes of angina pectoris and the possible mechanisms were presented clearly and carefully to the patient. He readily became certain of the associations and realized that it was imperative for him to change his reactions to his problems if he was to improve his health. Drugs were not prescribed, although he was advised to carry glyceryl trinitrate. For the two month period following the instructions he has not had another episode of angina pectoris and has not employed any glyceryl trinitrate, an experience for which he is exceedingly grateful. His electrocardiogram has remained normal.

Comment.—The experience of this patient definitely indicates the relationship of the psychic state to cardiac function. The angina pectoris syndrome with the typical electrocardiographic findings (fig. 1) are objective evidence of such relationships. It is obvious that a vicious cycle was in progress in which the number and severity of the attacks of pain were increasing and in turn were increasing his anxiety state, which in turn increased the episodes of angina pectoris, etc. Drugs certainly were not the means for interrupting the cycle; this could only be accomplished by proper measures directed at the psychic disturbances. Previous therapy with drugs failed, while psychotherapy resulted in dramatic improvement. There is no doubt that the patient is still experiencing some psychologic disturbances, but they have not been severe enough to produce pain. It is possible, however, that they are producing subtle cardiac dysfunction which might have some influence on his cardiac state in the future. It is obvious that such phenomena can occur, but unfortunately are difficult to study. From a practical clinical point of view it is preferable to manage the patient as though they are occurring and therefore must be avoided by careful psychiatric management. The extreme sensitivity of the peripheral blood vessels to psychic disturbances is shown in the plethysmograms in figures 2, 3, 4 and 5.

Case 2.—E. B., a white man aged 63, was examined because of pressing precordial pain with radiation down the left arm. The onset was four months prior to admission. He had previously had extramarital intercourse with a neighbor. He had no difficulty until his wife learned of this affair, and during the ensuing weeks the characteristic clinical picture of angina pectoris would develop each time the subject was mentioned by his wife. In addition, the sight of the extramarital partner or recalling his experiences would result in pain and typical electrocardiographic changes of depression of the S-T segment and inversion of the T wave during the attack. Between episodes the electrocardiogram was normal. His severance of relations with the neighbor as well as an understanding of the correlation of all factors and the psychosomatic mechanisms at work both in the patient and in his wife resulted in a disappearance of the angina pectoris. At present, discussion of his past experiences produces no anginal pain or measurable peripheral vascular response.

Comment.—The relationship of the angina pectoris to the psychic disturbances is evident. The patient had developed a conditioned response to his friend such that sight of her or a mere thought of the conflicts involved and his wife's reactions would precipitate pain. As in the preceding patient it was not drug therapy that was indicated but rather psychotherapy. After adequate discussions of the problems with him and his wife, the patient has not had another episode of angina pectoris. Both patients have shown considerable improvement in general physical and mental health, and are now happy.

Case 3.—T. L., a Negro man aged 54, was seen because of chronic ulcers on the tips of the fingers. He was well until one and one-half years before admission. Chronic ulcers developed on two of his finger tips which healed slowly. Six months before admission ulcers developed on several fingers. He was examined by a number of physicians and was informed that he had leprosy. The decision to enter a leprosarium for complete isolation resulted in much family turmoil, quitting a job, terminating a happy family life and a great deal of other unhappiness. He entered the leprosarium, where the diagnosis was not confirmed and he was promptly discharged. After spending three weeks in another hospital without a diagnosis, he became anxious and resentful. When first seen in consultation at Charity Hospital he was resentful to the point of being noncooperative. During the interview the classic digital syncope of Raynaud's disease developed in two finger tips. The remainder were cyanotic. The characteristic changes in color followed. These reactions were discussed with the patient. He became considerably relieved to have a definite diagnosis finally established. The second interview was much less disturbing, and his attitude was one of cooperation. When the diagnosis of leprosy was mentioned, however, digital arterial spasm occurred and the resultant digital syncope appeared instantly. The typical changes in color followed. After the normal color had returned the diagnosis of leprosy was mentioned again with almost instantaneous digital syncope and the reappearance of the entire syndrome. During the succeeding two weeks he was seen on several occasions and every time that reference was made to the diagnosis of leprosy classic digital syncope followed immediately. The mention of any event or person associated with the previous diagnosis resulted in digital syncope.

The subject had been a successful Pullman porter for thirty years, but the increasing demands of patrons resulted in extreme resentment. Discussion of impatient and demanding patrons resulted in digital syncope.

Comment.—The relationship between emotional disturbances and peripheral "angina" is obvious in this subject. He demonstrated a conditioned response to his past experiences about leprosy so that reference to the disease, physicians or hospitals associated with that experience resulted in spasm of the digital arteries. The nature of the illness and the psychosomatic mechanisms at work have been explained to the patient. On subsequent visits there was progressively less reaction to discussions related to his past experiences. His progress on psychotherapy alone has been satisfactory and his entire outlook has changed.

Case 4.—R. S. H., a white male medical student aged 22, was seen because of short paroxysms of extreme hypertension. The presence of hypertension was noted on routine examination. Later the blood pressure was normal on repeated examinations. He once noticed that thinking of sexual intercourse would result in an elevation of the systolic blood pressure to 200 mm. or more. Within a period of a few minutes the blood pressure would fall to within normal limits. The subject learned that he could elevate his blood pressure voluntarily by thinking of sexual intercourse and tensing the muscles of the perineum.

Plethysmographic studies were obtained while the patient was given the Rorschach test (fig. 2*C*). Throughout the test his blood pressure was elevated slightly and his pulse and alpha deflections were small, indicating vasoconstriction. He relaxed after this period and his blood pressure and pulse and alpha deflections returned to normal. He was asked to elevate his blood pressure again. Within a period of one minute his blood pressure rose from a normal level to 250 systolic and 150 diastolic. The pulse deflections were small and the alpha deflections practically disappeared, indicating pronounced vasoconstriction. His expression became apprehensive, his pupils

dilated and a severe bitemporal headache occurred. Within a short time the blood pressure returned to normal. The observation was interrupted by the subject's having to urinate, although the bladder was emptied one hour earlier. After the hypertension there was a large quantity of almost colorless urine of low specific gravity, whereas one hour earlier the urine was a normal amber color.

Comment.—The observations in this case further indicate the relationship of the mental processes to the state of the blood vessels. By an erotic thought the subject could purposely elevate his blood pressure. The extreme vasoconstriction is indicated by the small pulse and alpha deflections and the degree of hypertension. It is interesting that the process of relaxation was also under voluntary control, although a slightly longer time was required for the blood pressure to return to the resting level. The vasoconstrictor response was immediate and consistent. The effect on the kidneys was striking. The large volume of hyposthenuric urine is attributable to the increase in filtration pressure, probably due in part to constriction of the efferent arterioles of the glomeruli. The dilatation of the pupils indicates a diffuse sympathetic stimulation. Repeated reactions of this magnitude may be expected to result in organic vascular disease.

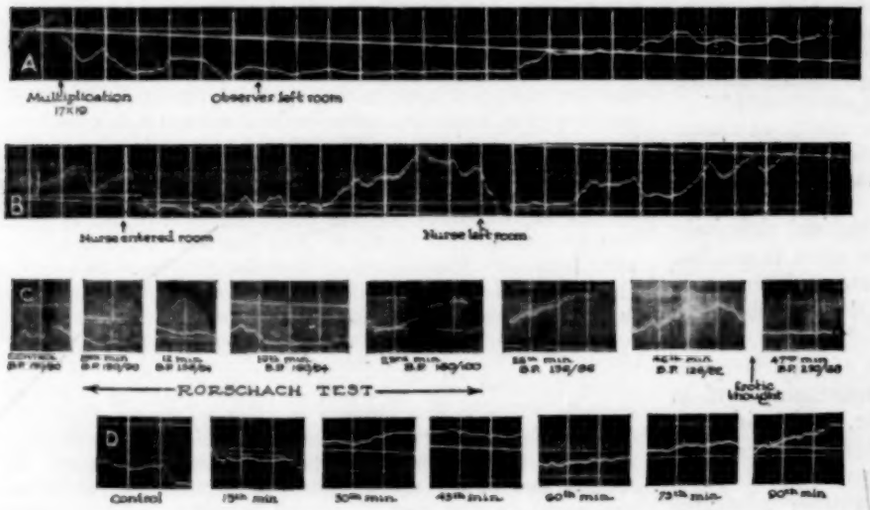

Fig. 2.—Plethysmograms obtained from the tip of the index finger of several subjects. *A*, prolonged vasoconstriction following a problem in multiplication by a normal subject. The pulse and alpha deflections are small indicating pronounced vasoconstriction. *B*, reaction to the entrance of a nurse into the normal subject's room. Both entrance and departure of the nurse resulted in vasoconstriction. *C*, plethysmogram on patient 4, who was able to produce decided hypertension voluntarily by an erotic thought. The control tracing shows normal pulse and alpha deflections. During the Rorschach test there is obvious vasoconstriction, the pulse and alpha deflections being small. The twenty-sixth and forty-sixth minutes demonstrate normal pulse and alpha deflections. The last plethysmogram recorded during the intentionally produced hypertension shows pronounced vasoconstriction. *D*, plethysmograms on patient 1, who had an episode of angina pectoris precipitated by an anxiety state. Plethysmograms taken at fifteen minute intervals show vasoconstriction throughout the entire period of observation. At no time during the study did the subject become relaxed. The patient had anginal pain during the early portion of the observation.

PLETHYSMOGRAPHY

During the course of plethysmographic studies on normal subjects and patients with various types of cardiovascular disease states, it became evident that the peripheral blood vessels are easily influenced by psychic disturbances. The development of a practical type of plethysmograph [14] has made it possible for others to search these problems. Psychosomatic studies directed at the peripheral blood vessels are important because of the possible relationship to disease states related to the cardiovascular system as well as to the psyche. Furthermore, it will be shown that plethysmography offers an objective approach to many problems in psychology and psychiatry.

The relationship of changes in the volume of the vascular bed to variations in the psychic state is not a new observation. It is only necessary to recollect the cardiovascular reactions associated with syncope produced by fear, a phenomenon as old as man himself. The studies of Burton,[15] Goetz,[16] Hertzman and Dillon,[17] Neuman and others,[18] Gottschalk,[19] Burch and coworkers[20] and others have shown the relationship of the behavior of the peripheral blood vessels to psychic function. It has been suggested[21] that a correlation of the five types of volume deflections (pulse, respiratory, alpha, beta and gamma) of the peripheral blood vessels may serve as an index of emotional states and types of personality. The exact patterns of the volume deflections related to the psychic states have been only partially observed.

It is well to remember that the peripheral blood vessels offer something somewhat unique in the approach to psychosomatic problems: (1) the peripheral vessels are extremely sensitive to mental processes of the conscious and subconscious levels; (2) they are readily accessible and (3) a sensitive and quantitative method (the plethysmograph) makes it practical to observe small and sudden vascular reactions. The peripheral blood vessels can serve as a useful tool as effector organs in psychosomatic phenomena.

14. Burch, G. E.: A New Sensitive Portable Plethysmograph, Am. Heart J. **33**: 48, 1947.

15. Burton, A. C.: The Range and Variability of the Blood Flow in the Human Fingers and the Vasomotor Regulation of Body Temperature, Am. J. Physiol. **127**: 437, 1939.

16. Goetz, R.: Rate and Control of Blood Flow Through Skin of Lower Extremities, Am. Heart J. **31**: 146, 1946.

17. Hertzman, A. B., and Dillon, J. B.: Selective Vascular Reaction Patterns in the Nasal Septum and Skin of the Extremities and Head, Am. J. Physiol. **127**: 671, 1939.

18. (*a*) Neumann, C.; Lhamon, W. T., and Cohn, A. E.: A Study of Factors (Emotional) Responsible for Changes in the Pattern of Spontaneous Rhythmic Fluctuations in the Volume of the Vascular Bed of the Finger Tip, J. Clin. Investigation **23**: 1, 1944. (*b*) Neumann, C.; Cohn, A. E., and Burch, G. E.: A Study of the Influence of the Character of an Examining Room on the Peripheral Blood Vessels of Normal, Hypertensive, and Senile Subjects, J. Clin. Investigation **21**: 651, 1942.

19. Gottschalk, L. A.: A Study of Conditioned Vasomotor Responses in Ten Human Subjects, Psychosom. Med. **8**: 16, 1946.

20. Footnote 7, Burch, G. E.; Cohn, A. E., and Neumann, C.: Reactivity of Intact Blood Vessels of the Fingers and Toes to Sensory Stimuli in Normal Resting Adults, in Patients with Hypertension, and in Senile Subjects, J. Clin. Investigation **21**: 655, 1942.

21. Burch, Cohn and Neumann,[7] Neumann, Lhamon and Cohn.[18a]

To illustrate the psychosomatic relationships of the peripheral blood vessels and psychic processes certain plethysmograms were recorded. Subjects were made to rest in bed in an air-conditioned room (not necessary for all types of studies, however), with temperature and relative humidity approximately 78 F. and 50 per cent, and plethysmographic recordings of the changes in vascular volume of the tips of the index finger and/or second toe were made as previously described.[14] The observation room was especially designed to reduce psychic disturbances to a minimum.[15b] The subjects studied were young men and women (medical students) who were normal or patients with known abnormal psychiatric states, usually anxiety neurosis. During the course of the recording of the plethysmograms psychic disturbances were produced by various methods, including entrance into the room, frowning at the subject, questioning the subject, dropping a book in an adjacent room, buzzing a buzzer, loud talking, multiplication of numbers, etc.

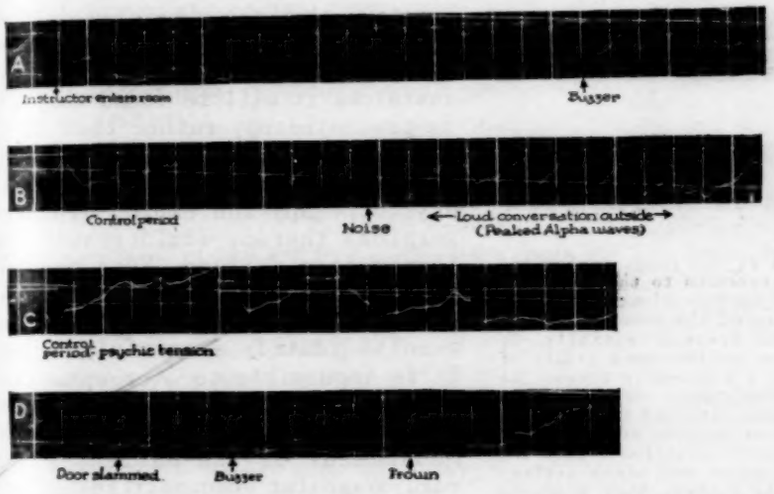

Fig 3.—Plethysmograms obtained from the tip of the index finger of normal subjects. *A*, reaction to the subject's instructor entering the room with resultant small pulse and alpha deflections indicating vasoconstriction. The peaked alpha deflections which followed suggest incomplete relaxation. The sound of a buzzer in the observation room produced vasoconstriction again. *B*, normal alpha waves during the control period followed by vasoconstriction in response to a noise in the adjacent room. Again, the high peaked alpha waves indicate incomplete relaxation, probably related to loud conversations outside. *C*, plethysmogram of a subject who was anxious at the onset of the observations. The pulse and alpha deflections are small throughout the record, indicating vasoconstriction. *D*, the same subject as *C*, fifteen minutes later. The pulse deflections in the first portion of the record are of normal size and indicate that a state of relaxation had been reached. Noises (door slammed across the hall and buzzer) resulted in vasoconstriction again with immediate return to the resting stage. When the observer frowned at the subject the reaction was more intense (smaller pulse and alpha deflections) and more prolonged.

All test stimuli evoked demonstrable reactions; i. e., reduction in the volume of pulse deflections and in total volume of the part. In addition, there were changes in the alpha deflections. They became smaller, more irregular and exhibited a more rapid rate of change than in a normal relaxed subject (fig. 3*B*).

Other determinants of the degree of the reaction are the nature and intensity of the stimuli. For example, informing a student that he has failed an examination produces a greater and more prolonged reaction than the pain of a pin prick. The degree of reaction can be measured in terms of the percentage change in the volume of the vascular bed and the duration of these changes.

Many patients have been observed who did not achieve relaxation (that is, they were in a state of psychic tension) during the entire period of observation (figs. 2*D* and 3*C*). As would be expected, the degree of reaction occurring in a person with preexisting vasoconstriction is less than that which occurs in a subject with vasodilatation before application of the stimulus (figs. 4*C* and 4*D*).

Furthermore, the failure of a person to become mentally at ease under conditions conducive to a state of relaxation of the peripheral blood vessels becomes recognizable through the medium of the plethysmogram in that the volume of the pulse and alpha deflections remains small and the character altered. An example of this is illustrated by figure 2*D*, which shows small alpha and pulse deflections throughout an entire period of observation of approximately two hours. Subjects who have been placed in a state of mental unrest by certain psychic influences to which they are rather sensitive will show a prolonged reduction in volume of alpha and pulse deflections. An example of this is shown in figures 3*A* and 4*A*, in which a student's instructor remained in the observation room. During this time the peripheral blood vessels reflected his psychic disturbances. After the instructor left the room the subject soon became mentally at ease and his pulse and alpha waves returned to normal volume and character (figs. 3*A* and 4*A*). These vascular reactions to mental unrest are further demonstrated by the fact that the mental processes concerned with simple multiplication resulted in a considerable and sustained decrease in the volume of alpha and pulse deflections (figs. 2*A* and 5*A*). These deflections did not return to normal until the process of multiplication had been completed. However, they again suddenly reduced in volume when the subject was seized with the idea that he had made an error in the calculations. When reassured of the accuracy of the multiplication, relaxation of the blood vessels followed (fig. 5*A*).

A self-induced psychic disturbance with pronounced vasoconstriction and hypertension was produced by one subject. This resulted in tachycardia, elevation of blood pressure to 250 systolic and 150 diastolic, marked diuresis and hyposthenuria and an intense bitemporal pain. These changes were brought about by an erotic thought. The plethysmogram was characterized by a considerable reduction in the volume of peripheral vessels of the finger and toe tips with the associated reduction of the pulse and alpha deflections (fig. 2*C*). These reactions were transient, being produced when the thought was brought to conscious levels

and disappearing when the thought was dismissed.

The rapid and acute peripheral vascular reactions to minor stimuli were produced in a number of subjects. These are summarized in figures 2, 3, 4 and 5. It can

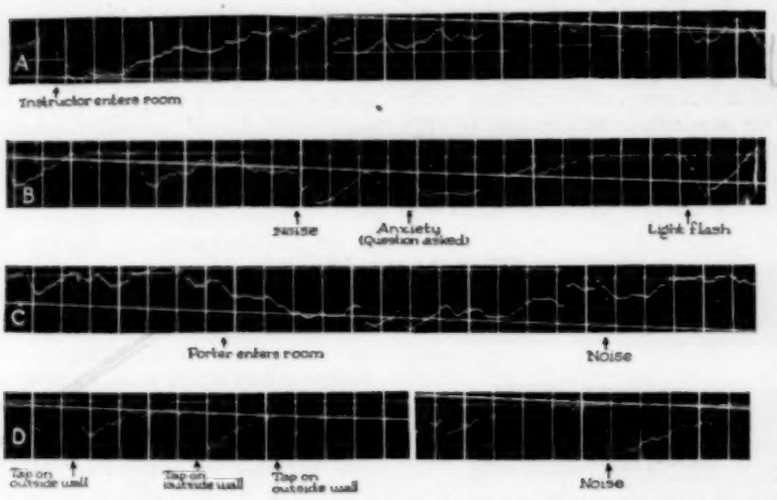

Fig. 4.--Plethysmograms obtained from tips of the incex finger and second toe *(C)* of normal subjects. *A*, decided reaction to the subject's instructor entering the room. The pulse and alpha deflections are small. The high peaked alpha waves in the last portion of the record indicate failure to return to the degree of relaxation present initially. *B*, reaction to noise, anxiety and light flash. The anxiety was a result of referring to an examination which the subject had recently taken. The vasoconstriction produced by the anxiety was of longer duration than the response to noise or light. *C*, plethysmogram obtained from the tip of the second toe of the subject in *B*. The first portion of the record shows normal pulse and alpha deflections. A porter's entrance into the room resulted in vasoconstriction and small pulse and alpha deflections. This reaction continued throughout the record. When a second stimulus (noise) was applied to a person already in a state of vasoconstriction little further reaction occurred. *D*, reactions to the same stimulus repeated at frequent intervals in subject of *B* and *C*. There was less reaction to the last stimulus, a sort of "tachyphylaxis." The reaction to noise by the same subject when the vessels were relaxed resulted in pronounced vasoconstriction.

be seen that there was a rapid emptying of the blood vessels of the fingers and toes evidenced by a decrease in total volume of the part as well as in the volume of pulse and alpha deflections when the stimuli were applied. For example, such stimuli as a noise, frowning at the subject by the observer and a pin prick resulted in demonstrable vascular responses.

GENERAL COMMENT

From the foregoing considerations, it is obvious that the cardiovascular system is responsive to psychic stimuli. This is true for both the central and the peripheral portions. In the past, these reactions have been followed by relatively limited methods; namely, the electrocardiograph, determination of blood pressure and general clinical observations. The plethysmograph increases our armamentarium. From the plethysmographic studies presented it becomes evident that the peripheral blood vessels of man are in a constant state of turmoil produced by the many variable environmental stimuli. For example, such simple disturbances as the entrance of a person into a subject's room will produce vasoconstriction. It then becomes a problem of differentiating the aspects of those reactions which are of fundamental nature in maintaining physiologic health from those which produce subtle but repeated wear and tear ultimately resulting in cardiovascular abnormalities.

From the point of view of the psychiatrist, these peripheral vascular reactions observed plethysmographically can serve as an objective and quantitative index of certain psychiatric and psychologic states. As mentioned previously there is a need for objective methods of following mental processes. The peripheral blood vessels serve as a sensitive effector organ, and a sensitive plethysmograph[14] as a simple and practical apparatus for recording these reactions.

It is evident from the case histories described that in the clinical management of a patient, particularly the patient with cardiovascular disease, it is imperative that the physician devote considerable time to an analysis of psychiatric problems. In many instances it will be found that it is psychotherapy rather than drug therapy which will produce desired clinical results. To neglect psychotherapy and employ drug or surgical therapy would result in therapeutic failure. Even though psychiatric analysis is time consuming, the rewards in therapeutic results justify a careful study. It is impossible to overemphasize the role of anxiety states and other psychiatric problems in the management of the patient with cardiovascular abnormalities.

SUMMARY

The cardiovascular system is particularly susceptible to psychic disturbances and it is the most commonly involved effector organ.

The central (cardiac) effects are numerous and include (1) increased cardiac output, (2) mechanistic disturbances, (3) electrocardiographic changes, (4) angina pectoris and (5) even sudden death.

The peripheral vascular system is extremely

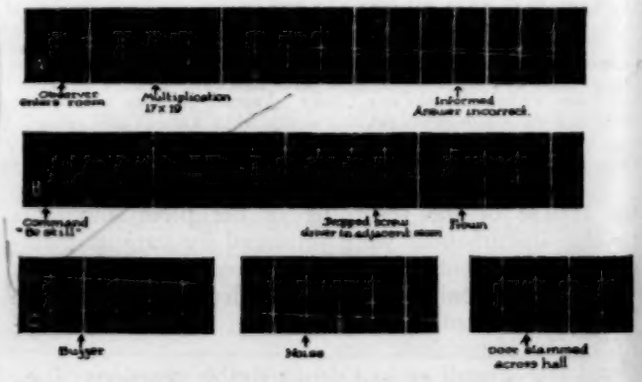

Fig. 5.—Plethysmograms obtained from tip of index finger in 3 normal subjects. *A*, the reaction to an observer entering room was slight. Considerable vasoconstriction resulted from a problem in multiplication. After the problem was completed, relaxation followed. When the subject was informed that the answer was incorrect an immediate vasoconstriction recurred. *B*, vasoconstriction resulted from a gruff command, "Be still!" The reaction to a frown was approximately of the same duration and intensity. The response to noise was short and not so great. *C*, vasoconstriction produced in 3 subjects by different stimuli.

responsive to the thought processes and emotional stimuli, and this portion of the cardiovascular system is readily accessible for qualitative and quantitative study.

A simple, accurate and quantitative method for study of the more subtle reactions has been described. The degree and duration of the vascular responses reflect the intensity of the emotional stimuli. Tense, unrelaxed subjects may be identified by the character of their plethysmogram. The potentialities of the plethysmograph in psychiatric evaluation are great. Its application as a new avenue of objective approach in psychiatry deserves further investigation.

Four case histories have been presented to illustrate the pronounced effect which disturbances in the psyche exert on the cardiovascular system. The need of psychiatric evaluation and the use of psychotherapy in the proper management of cardiovascular problems has been emphasized.

ABSTRACT OF DISCUSSION

Dr. George A. Wolf Jr., New York: I can add nothing to what has been observed, but I would like to speculate a little on the possibilities of such a method. It illustrates nicely that when we consider our patients to be in the basal state, during cardiovascular experiments with people walking in and out of the room and lights going on and off, they are not truly in the basal state, as far as their reactibility is concerned. One aspect of this problem is the reactibility of the same person at different times and the reactibility of different persons. In this regard what is the relationship of hypertensive to normal persons, early in their lives prior to the development of hypertensive disease, when hypertension becomes moderately developed and, later when they have advanced hypertension with outright vascular disease? A group of workers at the Rockefeller Institute have pursued this question. Would this method be of any value in deciding whether there is a real difference in the reactibility of peripheral blood vessels in these various phases of hypertension? As far as the psychologic phenomena are concerned, it would be of interest to determine whether a specific emotional state could be correlated with the reactibility of the blood vessels and the degree of reaction, inasmuch as the method described is a quantitative one. These are some of the things which might be pursued by this instrument. As Dr. Burch pointed out, a way to make progress in this field is to explore the physiology of so-called emotional states with every instrument available and attempt to associate the physiologic changes with the emotions.

Dr. Mandel E. Cohen, Boston: Little could be added to the description of the plethysmograph and the observations on it. Dr. Burch has conquered most of the difficulties in accuracy that have gone with this type of recording, with this new apparatus. This leaves us free to discuss the problem of the stimulus in this type of study and the general problem of drawing conclusions from this type of experiment. It is important to examine the general aspects, since many unproved assertions and broad generalizations are found in the medical field now called by some psychosomatic medicine. In studying the effect of an emotion-provoking stimulus on a measurement of physiologic function, it is important to ask whether the emotion-provoking stimulus is specific and crucial. But does any stimulus such as change of posture or slamming the door cause the same response? If talk stimulus causes the response, does any talk do it or must some special talk such as about special problems do it? For instance, we heard a report of a patient's changes in blood pressure associated with special problems about the patient, but in that report the author had neglected to say what happened if one just talked about anything. It is good to use plain language and not pretentious psychologic talk. Finally, we must be careful about conclusions. If we attempted to say that emotions cause hypertension because they cause blood pressure to go up—well, putting the hand in ice water also causes the blood pressure to go up, and it would be just as plausible to say that ice water causes hypertension. If experiments are so difficult to draw conclusions from, how much harder is it to interpret a patient's history to connect emotion-provoking situations with symptoms of disease? We must know whether the reported experience is accurate. Did it relate in time to the symptom? Did the experience cause the disease, or was it merely one of many factors that may have provoked symptoms? Or did the disease itself lead to the emotional disturbance? This aspect of medicine is still a mass of unproved assertions. Our attitude toward work in this field should be the same as in other parts of medicine. We should not neglect the possibilities, nor should we be gullible, to accept without adequate evidence, sufficient cases or adequate controls speculations and conclusions related to the reaction or emotion-provoking stimuli to disease. Even if the magical word "psychosomatic" beckons us, we can still demand cold facts before accepting the conclusions.

Dr. George E. Burch, New Orleans: As stated, this was not an organized attempt to solve the characteristic plethysmographic patterns that might be specific for any one type of psychic disturbance. We have always been impressed by the ease with which these vascular reactions occur after some of the minor, ordinary and everyday psychic experiences. We feel that the problem of plethysmography is essentially where electrocardiography was about 1900. There are many vascular patterns which have not been described. There is a great opportunity for the psychiatrist to approach many of his problems through the peripheral blood vessels as organs reflecting psychosomatic phenomena.

MANAGEMENT OF PROTEIN DEFICIENCY IN SURGICAL PATIENTS

Intravenous and Intrajejunal Injections

JOHN D. STEWART, M.D.
HARRY W. HALE Jr., M.D.
and
SIDNEY M. SCHAER, M.D.
Buffalo

Though protein nutrition is important in any field of medicine it is of special concern to the surgeon. The surgeon is often charged with the care of a depleted patient who must undergo a major surgical procedure as part of his treatment. In many instances obstructing or inflammatory lesions of the gastrointestinal tract preclude adequate oral alimentation. Superimposed on an accumulated nitrogen deficit may be losses of protein through draining wounds and sinuses, into areas of inflammation and into traumatized tissues, and losses from hemorrhage; the "reaction of injury" involving an ill understood increase in the rate of protein catabolism often inevitably complicates the problem for the surgeon. Furthermore, the hazards of protein deficiency during convalescence from surgical operation have come into clearer recognition as the subject has received closer study.

Despite the fundamental contributions of numerous investigators of protein metabolism and the adaptation of basic facts to clinical problems, various questions remain unanswered. For example, the possible increase in the need of specific amino acids or amino acid mixtures as occasioned by specific diseases is an obvious question which might repay study by qualified investigators. The present paper is concerned with some of the more practical aspects of protein nutrition in surgical patients. For the patient who cannot eat and who needs

From the Department of Surgery, University of Buffalo Medical School, and the Edward J. Meyer Memorial Hospital.

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protein and other nutrients desperately before and after operation how is the need to be met? As the result of various studies in recent years[1] much can be done in the management of such a clinical problem, though all the difficulties have by no means been eliminated.

In many cases the only feasible method of introducing protein in any quantity into the patient is by intravenous injections. For this purpose whole blood, plasma, serum, concentrated plasma fractions, synthetic mixtures of amino acid and protein hydrolysates may be used. Whole blood, plasma and hydrolysates of proteins of high biologic value have been most widely used to supply protein intravenously, and their usefulness is uncontested. For practical reasons particular interest centers on protein hydrolysates as a source of essential amino acids given by the intravenous route, and personal experience with this method will now be analyzed.

There are certain definite requirements to be met by the solution of amino acids to be used intravenously, and these may be listed as follows:

1. The aqueous solution must be stable.
2. It must contain the essential amino acids, each in suitable concentration.
3. It must produce only minimal changes in acid-base balance.
4. It must produce only minimal changes in water balance.
5. It must be nontoxic and nonallergenic, and it must be capable of being sterilized.
6. It must be inexpensive and readily available.

These specifications seem to be met reasonably well by enzymic digests of casein. The material which we have used ("amigen"),[2] consists of a sterilized aqueous nonpyrogenic 5 per cent solution of an enzymic hydrolysate of purified casein and pork pancreas to which dextrose has been added in 5 per cent concentration. The nitrogen of the solution is present chiefly as nitrogen of amino acids and polypeptides, and the solution supports nitrogen balance in man. The hydrogen ion concentration of the solution is adjusted to a value of 6.5. A liter of the solution, which supplies 50 Gm. of amino acids as well as 50 Gm. of dextrose, is given intravenously once or twice a day. Not less than three hours should be taken for the injection, for it has been shown that the more rapidly the solution is administered the greater the likelihood of reaction.

Such an enzymic casein hydrolysate may be used with advantage in a variety of conditions, and it may be given to the same patient repeatedly over a long period. In table 1 are shown data illustrating this point.

TABLE 1.—*Results of Injection of Twenty or More Liters of Amino Acid Solution (Amigen)*

Patient	Diagnosis	Amount, Liters	Time, Days	Reaction
H. A.	Gastric hemorrhage	36	46	None
F. B.	Cirrhosis and ascites	29	26	Venous thrombosis at injection site
F. L.	Carcinoma of rectum	38	95	Nausea with third infusion
H. O.	Intertrochanteric fracture; decubitus ulcers	25	28	None
G. R.	Multiple intestinal fistulas	90	90	Chill, nausea and vomiting with infusions 44, 88, 89 and 90
N. W.	Perforated gastric ulcer and peritonitis	38	60	None
M. D.	Chronic ulcerative colitis	32	21	None
I. H.	Gangrene of foot	21	24	None

One patient received as many as 90 liters of the solution over a period of three months. The incidence of untoward reactions in our experience was about 6.5 per cent, but serious reactions were lacking. Nausea and vomiting sometimes occur during the infusion, a reaction difficult of explanation though glutamic acid has specifically been indicted. Allergic reactions rarely occur, but pyrogenic effects are less rare, as seen in table 2.

TABLE 2.—*Reactions to Enzymic Casein Hydrolysate Given Intravenously (Amigen)*

Number of patients	166
Number of infusions	829
Number of reactions	54
Reaction rate per infusion	6.5%
Average amount per patient	8.6 liters
Type of reaction	
(a) Pyrogenic	33
(b) Allergic	2 (?) "
(c) Nausea	16
(d) Thrombosis of vein	3

A theoretic advantage of amino acid solutions over whole blood or plasma as an intravenous source of nitrogen is the free diffusibility of amino acids. Plasma protein when given in large amount may augment circulating blood volume undesirably and increase the cardiac work load. In chart 1 appear data indicating the rapidity with which amino acids are diffused out of the blood stream even when amounts as large as 100 Gm. are given in six hours.[3] Obviously the concentration of amino acids in the plasma after such infusions will depend on a number of factors besides diffusibility, including body fluid available for their dilution, rate of excretion in the urine and rate of conversion of amino acids into body protein or catabolic derivatives. A definite lowering of the carbon dioxide combining power of the plasma is a uniform finding after infusion of amino acids in quantity, even though the *p*H of the solution has been brought to 6.5 by the addition of base. This point may be of some importance for the severely dehydrated and acidotic patient.

It is of interest that no significant differences are noted in the concentration of amino acids and total nonprotein nitrogen in the plasma and urine between patients with severe hepatic disease and normal persons

1. Elman, R.: Parenteral Alimentation in Surgery, New York, Paul B. Hoeber, Inc., 1947; Maintenance of Nitrogen Balance by the Intravenous Administration of Plasma Proteins and Protein Hydrolysates, Physiol. Rev. **24**: 372, 1944. Mueller, A. J.; Fiekas, D., and Cox, W. M., Jr.: Minimum Maintenance Requirement of an Enzymic Casein Hydrolysate, Bull. Johns Hopkins Hosp. **72**: 110, 1943. Altschuler, S. S.; Hensel, H. M.; Hecht, P., and Pursley, R.: Maintenance of Nitrogen Equilibrium by Intravenous Administration of Amino Acids: Clinical Studies, Arch. Int. Med. **70**: 749 (Nov.) 1942. Mulholland, J. M.; Co Tui; Wright, A. M., and Vinci, V. J.: Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence: Study of Eight Patients Undergoing Partial Gastrectomy for Duodenal Ulcers, Ann. Surg. **117**: 512, 1943. Raydin, I. S.: Hypoproteinemia and Its Relation to Surgical Problems, Ann. Surg. **112**: 576, 1940. Cox, W. M., Jr.; Mueller, A. J.; Elman, R.; Albanese, A. A.; Kenumerer, K. S.; Barton, R. W., and Holt, L. E., Jr.: Nitrogen Retention Studies on Rats, Dogs and Man: The Effect of Adding Methionine to an Enzymic Casein Hydrolysate, J. Nutrition **33**: 437, 1947. Cox, W. M., Jr., and Mueller, A. J.: The Relative Efficiency of Different Forms of Intravenously Administered Nitrogen on Nitrogen Balance and Amino Acid Excretion, J. Nutrition **31**: 581, 1946. Madden, S. C., and Whipple, G. H.: Plasma Proteins: Their Source, Production and Utilization, Physiol. Rev. **20**: 194, 1940; Hemoglobin and Plasma Proteins: Their Production, Utilization and Interrelation, Am. J. M. Sc. **203**: 477, 1942.

2. Stewart, J. D., and Rourke, G. M.: Changes in Blood and Urine After Intravenous Amino Acid Mixtures in Patients with Liver Disease, Proc. Soc. Exper. Biol. & Med. **51**: 364, 1942.

after infusions. Graphic evidence on this point appears in charts 2 and 3. In a considerable experience with the intravenous administration of casein hydrolysate in grave hepatic disease we have found nothing to contraindicate such therapy. In chart 1 the rapid reduction in concentration of plasma amino nitrogen after intravenous infusion of large amounts is shown. No significant difference is observed between patients with severe hepatic disease and those without such disease.

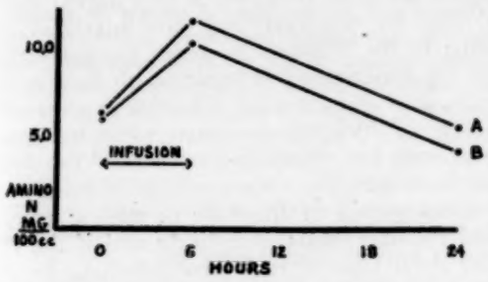

Chart 1.—Plasma amino acid concentration before and after infusion of 1,000 cc. of a 10 per cent solution of amino acid (amigen). Line *A* refers to 6 patients with severe hepatic disease and line *B* to 2 normal persons.

In chart 2 is depicted the urinary excretion of amino nitrogen and total nitrogen in a normal person during and after intravenous infusion of a total of over 6 Gm. of amino nitrogen. The casein hydrolysate used was given at an increasingly rapid rate over a six hour period. In chart 3 data from a similar study on a patient with hepatic failure from toxic hepatitis are shown. The patient with hepatic disease apparently retained somewhat less of the injected amino nitrogen during the short period of the study, but no depression of the deaminization function is evident.

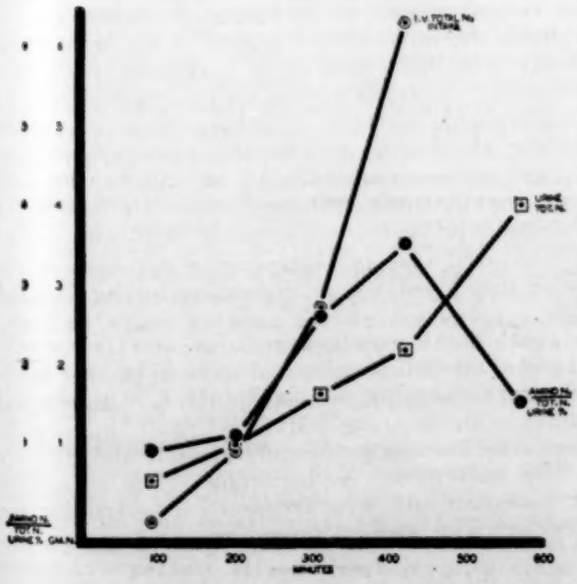

Chart 2.—Effects of infusion of amino acids in a normal person.

The value of intravenous infusions of casein hydrolysates in the light of experience to date would seem to lie in the fact that they supply a patient whose ability to eat and digest protein is limited with the essential amino acids in reasonably adequate amounts. Repair of nitrogen deficits, particularly in connection with major surgical procedures, can be facilitated in this manner. It is hardly necessary to point out that the administration of 1 or 2 liters of a 5 per cent solution of amino acids and a 5 per cent solution of dextrose per day does not constitute nutritional maintenance. The need for calories, vitamins and minerals must be met, and the extent to which the other cardinal nutrients are supplied may well influence the utilization of the amino acids given. Obviously amino acid solutions are not substitutes for blood transfusions, though they furnish the body with some of the essential elements for hematopoiesis. The importance of iron in this connection must be kept in mind by the surgeon.

In many cases of chronic lesions of the esophagus, stomach and duodenum intrajejunal feeding is of life-saving value. Obstructing and inflammatory lesions of these organs may result in rapid loss of weight and general malnutrition, and the patient may be in poor condition for the major corrective operation required. Preliminary jejunostomy and a period of hyperalimentation before operation are often essential to the success of surgical intervention in this region. Supplementary jejunostomy done at the time of the definitive operation and transorogastric tube feeding are also necessary at times, but it is usually desirable to restore nutrition before operation whenever possible as well as afterward during convalescence.

Jejunostomy is done in our practice by a modified Witzel technic under local anesthesia, a no. 16 F catheter being used.[3] If properly performed, the jejunostomy

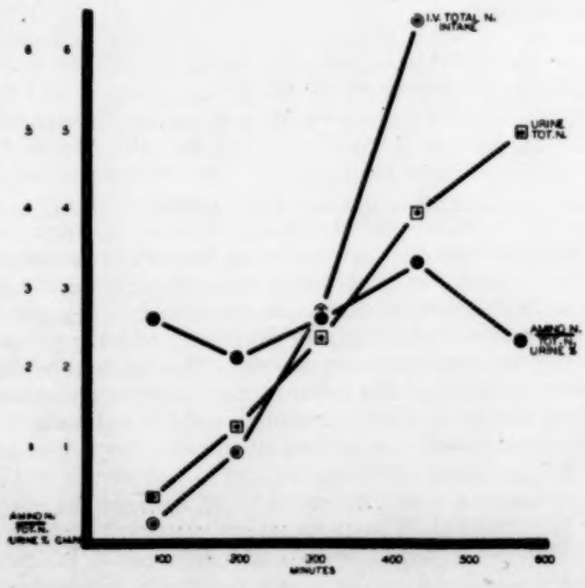

Chart 3. Effects of infusion of amino acids in a patient with hepatic failure due to toxic hepatitis.

opening does not leak and it closes immediately on removal of the catheter. If precautions are taken to keep the catheter strapped in place, it may be used for months if necessary. Intestinal obstruction at the site, leakage and peritoneal contamination do not occur if the jejunostomy is properly executed. When it is possible to choose a site the jejunostomy should be done about 18 to 24 inches (46 to 61 cm.) below the ligament of Treitz so that sufficient free jejunum is left proximally for subsequent procedures. Intrajejunal alimentation has the important advantage of enabling the patient to take a complete dietary mixture so that not only protein is supplied in large amount but the other essential nutrients as well. One patient with an esophageal lesion took the formula to be described intrajejunally for over

3. Linton, R. E.: Enterostomy, Am. J. Surg. 25: 55, 1934.

six months as the sole source of food, and weight and sense of well-being were maintained. For many of our patients intravenous and intrajejunal alimentation are used concurrently.

A satisfactory mixture for intrajejunal feeding must fulfil certain requirements, and in our judgment these may be set down as follows:

1. The mixture should be complete and should supply in adequate amount the elements of the normal diet.
2. It should be fluid enough to drip by gravity through a small catheter (no. 16 F.) without undue sedimentation.
3. It should be neutral in reaction or approximately so.
4. It should contain enough colloid to protect the intestinal mucosa against irritant "salt action."
5. It should be inexpensive and easily prepared.
6. It should be capable of being varied to meet individual needs.
7. It should yield a low residue during digestion and absorption.
8. It should be easily digested and absorbed.
9. It should keep at least forty-eight hours in the refrigerator.

A formula which meets these criteria reasonably well and which we have used for the last six years is detailed in table 3.

TABLE 3.—*Formula for Intrajejunal Feeding*

		Salt Mixture	
Water	2,500 cc.		
Sucrose	300 Gm.		
Casein	200 Gm.	$CaCO_3$	20.0
Dried yeast	30 Gm.	$NaH_2PO_4 \cdot H_2O$	16.0
Trypsin	5 Gm.	KCl	28.0
Vitamin C	100 mg.	$MgCO_3$	6.0
Halibut liver oil	1 Gm.	Na_2CO_3	6.0
Vitamin K	4 mg.	Fe Amm. citrate	6.0
Salt mixture	16 Gm.	NaCl	18.0

In the preparation of the mixture the casein is added slowly to the water while being brought into even solution with the help of a mechanical mixer. The casein is obtained in 25 (9 Kg.) or 50 pound (22 Kg.) lots, with a considerable saving in cost. The fat, and hence the caloric value, of the mixture can easily be increased by the addition of olive oil, cream or corn oil as indicated.

Chemical analysis of this mixture gives the following results:

Average total weight	2,543 Gm.
Average total volume	2,395 cc.
Percentage of moisture by weight	78
Percentage of solids by weight	22
Percentage of dry ash by weight	0.75
Specific gravity	1.068
Total protein content (nitrogen × 6.25)	196.5 Gm.
Total chloride content	3.9 Gm.
Total sodium content	
determined directly on sample	4.1 Gm.
determined on ash	4.1 Gm.
Total calcium content determined on ash	1.1 Gm.
Total phosphorus content determined on ash	4.7 Gm.
Total potassium content determined on ash	1.9 Gm.
pH (fresh and after four days at 4 C.)	6.2
Total fat content (ether 1-petroleum ether 1)	5.08 Gm.

This mixture is given each day by gravity drip, preferably continuously over a twelve hour period. If the patient is ambulatory the administration can be carried out during the night without disturbance of his sleep. If the solution is injected intermittently care must be used not to instil too much at one time, since distention of the jejunal loop, nausea or cramps and diarrhea may occur. Three or 4 ounces (90 or 120 Gm.) instilled into the jejunostomy catheter every half hour during the day may be employed, and in many instances the patient learns to do this himself, with a consequent saving in nursing time. Continuous administration of the formula by gravity drip during the night is the method to be preferred, as the patient is thus freed for studies or for ambulation during the day. Occasionally the feedings provoke diarrhea, in which event temporary suspension of the method or reduction in the amount administered together with injection of paregoric into the jejunostomy gives relief. In other instances the mixture is found to be constipating.

Our experience with intrajejunal alimentation has included observance of cases of esophageal carcinoma treated later by resection, and particularly of cases of carcinoma of the stomach in which there was involvement of the cardiac end. Patients with pyloric obstruction due to carcinoma or ulcer and patients with obstructing or bleeding duodenal ulcer have at times been prepared for definitive gastric resection by intrajejunal feeding. The jejunostomy opening may be closed from within at the time of gastric resection if technical considerations so indicate and if the patient's need for such feeding has been relieved. In cases of pyloric or duodenal obstruction we do not advise reinjection into the jejunostomy opening of aspirated gastric secretions, as such fluid may be laden with bacteria and its volume interferes with the intrajejunal administration of the more nutritious formula.

In cases of obstructive jaundice and hepatic damage there is reason to believe that the high protein, low fat mixture described may be beneficial, and clinical experience with such cases confirms the belief. The method has been used chiefly for feeding during convalescence after pancreaticoduodenectomy, the jejunostomy having been done at the time of the definitive operation. It is undoubtedly desirable to have the patient take such a dietary mixture before as well as after pancreaticoduodenectomy, and this can be accomplished by feeding by drip through an inlying nasogastric tube before operation. It has seemed to us technically undesirable to complicate the problem of resection of the head of the pancreas and duodenum by a previously performed jejunostomy. There is a place for this method in cases of complicated stricture of the common duct with recurring cholangitis and hepatic damage,[4] and the usefulness of intrajejunal feeding in patients with malfunctioning gastroenterostomy stomas—fortunately a less common problem nowadays—has been pointed out.[5] The occasional case of postoperative duodenal fistula likewise may constitute an indication for intrajejunal feeding.

In conclusion it may be stated that:

(1) in the practical matter of meeting protein needs of surgical patients intravenous infusions of amino acid mixtures with dextrose and intrajejunal injection of a more complete dietary mixture are safe and effective and (2) such therapy is important before as well as after operation and it is frequently essential for the success of major surgical procedures.

ABSTRACT OF DISCUSSION

DR. I. S. RAVDIN, Philadelphia: More work of the type which Dr. Stewart and his group are doing is necessary before the best mixtures for oral or parenteral use can be available. It is highly likely that under varying needs a single solution will not adequately answer all the requirements to an optimal degree. Most of the nutritional deficiencies in man are complex deficiencies,

4. Stewart, J. D.: Gravity Feeding by Jejunostomy, Ann. Surg. 96: 225, 1932.

5. Allen, A. W., and Welch, C. E.: Jejunostomy for Relief of Malfunctioning Gastroepterostomy Stoma, Surgery 9: 163, 1941.

involving more than a single dietary component. In correcting a nutritional deficiency by any route, it is important to provide not only a balanced ration but also sufficient calories. We have talked too freely about the essential amino acids. It has been shown by Rose that they are essential for the growth of the rat and that when given in adequate amounts to man as the sole source of exogenous protein along with other dietary components a positive nitrogen balance can be achieved. Under certain conditions of disease or injury, when endogenous protein metabolism is disturbed, the problem is probably not so simple. While intravenous injections are often necessary as the sole source of dietary intake, it should be remembered that when the oral, orogastric or jejunal method of feeding can be used it is extravagant and wasteful to use the intravenous route. Riegel and her associates, working in our laboratories, have found that a positive nitrogen balance can be achieved in patients who have undergone a major operation when 0.3 Gm. of nitrogen and 30 calories per kilogram of body weight are given by any oral method but that nearly twice as much nitrogen is required with the same caloric intake when the intravenous route is used. The data of Madden are essentially in agreement with those of Riegel. The aim of any feeding program must be to achieve a positive nutritional balance. This is most easily and least expensively obtained by one of the direct alimentary methods. Dr. Stewart's work substantiates this statement. While it is possible to achieve a positive nitrogen balance by intravenous therapy if this is carefully controlled, it frequently is not achieved. To the extent to which a positive nutritional balance is achieved in patients, a corresponding decrease will be observed in the complications of anesthesia and operation.

Dr. Robert Elman, St. Louis: I have some data on patients who were kept on total intravenuous feeding after abdominal operation on a daily intake of 100 Gm. each of "amigen" and dextrose. In patient, after an extensive resection for jejunal ulcer, there was almost positive nitrogen balance. The net loss on one or two days was only 2 or 3 Gm. Patient, with injections of dextrose alone, would have shown a loss of at least 12 to 20 Gm. of nitrogen a day. In this patient I resected multiple intestinal fistulas and part of the abdominal wall, with primary anastomosis and closure. Note the positive nitrogen balance on six postoperative days even though the nitrogen intake on four of those days was very small (6 Gm.). Data were obtained during seventy-six days after serious abdominal operations. Caloric intake, because of the administration of 100 Gm. of dextrose, was 400. "Amigen" intake was 100 Gm. Note that the average loss of nitrogen was only 3.7 Gm. a day. Anyone who has studied these cases realizes that under the usual regimen or dextrose alone the loss varies between 10 and 20 Gm. of nitrogen a day. Thus it is clear that nitrogen balance or, at the worst, minimal losses will occur in many cases after operation with the daily injection of only 100 Gm. of hydrolyzed protein even when the caloric intake from dextrose is restricted to 400.

BRONCHOGENIC CARCINOMA.—The treatment of bronchogenic carcinoma consists of pneumonectomy with extirpation of the mediastinal nodes. It is our belief that it is just as essential to perform a pneumonectomy and to completely extirpate the mediastinal nodes in a patient with a bronchogenic carcinoma as it is to remove the entire breast and axillary nodes in a patient with carcinoma of the breast. Whereas there are some surgeons who believe that lobectomy is indicated in certain cases of malignant disease of the lung, we are of the opinion that lobectomy has little if any place in the treatment of primary malignancy of the lung. Only by the radical pneumonectomy with complete extirpation of the mediastinal nodes can good results be expected in the treatment of these neoplasms.—Ochsner, DeBakey, and Dixon, J.; Primary Malignancy of the Lung, *South Dakota Journal of Medicine*, February 1948.

RAPID TEST FOR THE DEMONSTRATION OF SICKLE CELLS AND ITS CLINICAL SIGNIFICANCE

KARL SINGER, M.D.
and
SIDNEY ROBIN, M.D.
Chicago

The various factors which cause or influence the phenomenon of sickling red cells are still poorly understood. This peculiar behavior of certain red blood corpuscles seems to be a racial characteristic, confined exclusively to the Negro, although a few cases of sickle cell anemia in white persons have been reported.[1] From what is so far known, one must assume that sickling will only occur in the presence of a fundamental alteration in the physicochemical structure of the erythrocyte, since normal cells cannot be induced to undergo such a change in shape. This constitutional structural defect is already demonstrable in the hemoglobin-containing erythroblast.[2]

Hahn and Gillespie [3] made the significant discovery that distortion of the susceptible corpuscles into sickle cells will only take place if the hemoglobin contained in the cells is in the reduced state. Presence of oxyhemoglobin or carbon monoxide hemoglobin prevents the sickle cell phenomenon. If sickled cells are exposed to a sufficient oxygen concentration they revert immediately to their original form. By means of a gas chamber into which susceptible red cells are suspended in a hanging drop of saline solution, the erythrocytes can be transformed at will by admission of alternating streams of carbon dioxide or oxygen into the chamber. Although this ingenious method is too elaborate for routine clinical use,[4] the principle established by it—namely, that sickling will develop only in the presence of reduced hemoglobin—forms the basis of all other tests which have been advocated for the detection of the sickling trait.

Diggs and Pettit [4] in 1940 compared all recommended technics and concluded that the moist stasis test of Scriver and Waugh [5] is the most reliable and the most practical method. In this test anoxia is produced by placing a rubber band around the proximal portion of a finger. Stasis is maintained for five minutes. Then the finger is punctured in the usual way and a drop of the dark blood is sealed under a cover slip as rapidly as possible. The greatest disadvantage of this method is the unavoidable partial reoxygenation of the hemoglobin due to exposure to air when the blood is transferred from the finger to the slide.

From the Department of Hematologic Research and the Kunstadter Laboratory for Pediatric Research, Michael Reese Hospital.

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1. Greenwald, L.; Spielholz, J. B., and Litwins, J.: Sickling Trait in a White Adult Associated with Hemolytic Anemia, Endocarditis and Malignancy, Am. J. M. Sc. **206**: 158-168 (Aug.) 1943. Morrison, M.; Samwick, A. A., and Landsberg, E.: Sickle Cell Anemia in the White Race: Report of Two Cases with Diagnosis by Splenic Puncture, Am. J. Dis. Child. **64**: 881-887 (Nov.) 1942.

2. Sydenstricker, V. P.; Mulherin, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children, with Necropsy in One Case, Am. J. Dis. Child. **26**: 132-154 (Aug.) 1923.

3. (*a*) Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia: Report of Case Greatly Improved by Splenectomy; Experimental Study of Sickle Cell Formation, Arch. Int. Med. **39**: 233-254 (Feb.) 1927 (*b*) Hahn, E. V.: Sickle Cell (Drepanocytic) Anemia, with Report of Second Case Successfully Treated by Splenectomy and Further Observations on Mechanism of Sickle Cell Formation, Am. J. M. Sc. **175**: 206-217 (Feb.) 1928.

4. Diggs, L. W., and Pettit, V. D.: A Comparison of Methods Used in the Detection of the Sickle Cell Trait, J. Lab. & Clin. Med. **25**: 1106-1111 (July) 1940.

5. Scriver, J. B., and Waugh, T. R.: Studies on a Case of Sickle Cell Anemia, Canad. M. A. J. **23**: 375-380 (Sept.) 1930.

Since mature red cells do not themselves consume oxygen, reduction of the oxyhemoglobin must necessarily depend on the oxygen consumption of the variable number of nucleated red cells, reticulocytes and leukocytes available in the sealed preparation. It is therefore not astonishing that sickling may sometimes be demonstrable only after forty-eight to seventy-two hours.

Rather recently Neuda and Rosen [6] reported a new rapid method for the demonstration of the sickling phenomenon. By mixing blood with a broth culture of a saline extract of human feces they could elicit the characteristic distortion of the susceptible erythrocytes within the first hour after preparation of this mixture. They attributed the enhancing of the sickling process to a—hypothetical—cell-damaging factor of enzymatic nature which is supposed to be present in the stool extract.

In this paper we want to describe a method which induces the sickling process in five to fifteen minutes with invariable regularity. The test is based on the principle of suspending the suspected erythrocytes in a culture of nonpathogenic bacteria and then sealing the preparation. The living organisms consume oxygen rapidly and also give off carbon dioxide, thus creating the most favorable conditions for the detection of sickling tendencies.

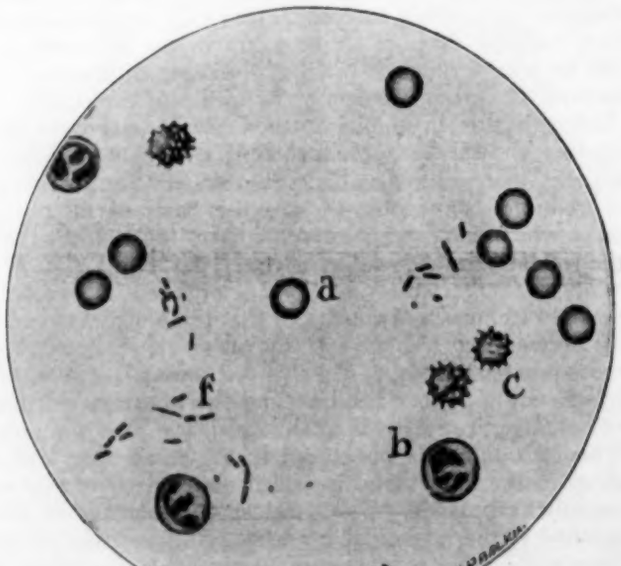

Fig. 1.—Rapid test negative in result: (*a*) red cell; (*b*) white cell; (*c*) crenated red cell; (*f*) bacteria.

Fig. 2.—Rapid test positive in result: (*a*) red cell; (*b*) white cell; (*c*) crenated red cell; (*d*) oat cell; (*e*) sickle cell; (*f*) bacteria.

TECHNIC OF THE RAPID BACTERIOLOGIC TEST FOR THE SICKLING PHENOMENON

The reagent used in performing the rapid bacteriologic test is a turbid culture of Bacillus subtilis grown in dextrose veal broth. B. subtilis was selected because of its high oxygen consumption and its established nonpathogenicity. Cultures of Escherichia coli and Aerobacter aerogenes were found to be almost equally effective. An active reagent was usually obtained by inoculating 4 cc. of broth with a loop of pure subtilis culture grown on an agar slant medium. The broth was then kept in the incubator for several hours at a temperature of 37 C. When inoculation was performed in the late afternoon, the test fluid was ready for use next morning. During the day the broth culture was allowed to stand at room temperature in order to avoid overgrowth, which easily occurs when the culture is kept in the incubator too long. Such an improperly prepared reagent is characterized by diminished or absent motility of the bacteria. For this reason ripening of the culture over the weekends was also obtained at room temperature. Perpetuation of the bacterial reagent can be accomplished by placing each day a few drops of the used broth culture into fresh broth medium. However, that cannot be continued indefinitely, since the bacteria become increasingly sluggish and show signs of deterioration after a few days. Reactivation of the reagent culture must be performed at least once a week by inoculating from an agar slant. Before each performance of the rapid test one must be sure to have an active reagent. Such an active test fluid is characterized by gross turbidity, absence of any precipitate or pellicle in the culture tube and microscopically by numerous actively motile bacteria. Furthermore, hemolysis of the red cells in the preparation within thirty minutes to two hours is also indicative of an effective culture. Although the necessity of caring for the perpetuation of the culture reagent in order to have it ready for use at all times represents the "weak point" of the rapid test, actually it causes little trouble if properly performed and requires but a few minutes per day.

Blood may be obtained by puncturing the finger in the usual way, or oxalated venous blood can also be used. If the blood sample has been kept in the refrigerator, it should be warmed before the test is performed, as chilling of the blood causes a prolongation of the reaction time.

The actual performance of the test is simple. One drop of blood and 1 drop of culture are mixed on a clean slide by means of a glass rod and then covered with a cover slip. The preparation should be free from air bubbles. The edges of the cover slip are sealed with paraffin and the slide is then placed into the incubator at 37 C. for five minutes. If the reading of the preparation shows no presence of sickling tendencies, the slide is again placed in the incubator for ten minutes, and then reevaluated. If after fifteen minutes no characteristically distorted erythrocytes are noted, the result of the test can safely be reported as negative.

However, one must keep in mind that the reaction time in this technic depends on three factors: the "activity" of the test fluid, the temperature and the intracorpuscular forces responsible for the sickling phenomenon. If the first two con-

6, Neuda, P. M., and Rosen, M. S.: Preliminary Report on a Rapid Method for Diagnosing Sickle Cell Disease, J. Lab. & Clin. Med. 30: 456-458 (May) 1945.

ditions are kept at an optimum, the third variable is of surprisingly little significance. In this respect the bacteriologic test differs remarkably from the moist stasis method, in which the inherent sickling tendencies of the red cells play probably an important role.

Reading of the preparations should not present any real difficulties if the oil immersion lens is used. Figure 1 visualizes a test which is negative in result. In this preparation the red cells are often crenated because the test fluid is not isotonic. In a test with positive result (fig. 2) one may see either the true sickle cells (fig. 2*e*) or cells which are not crescent shaped but look very distorted on account of variable filaments and finlike appendages which protrude from the surface of the cell (fig. 2*d*). We have applied the designation oat cells [7] to all these noncrescentic cells. They can probably be considered as precursors of the true sickle cells. Their presence is absolutely pathognomonic for the sickle cell phenomenon. It is perhaps conceivable that some of the oat cells may be confused with crenated erythrocytes. However, the protrusions of the crenated cells are equally spaced and of equal length, whereas those of the oat cells are irregularly spaced and of variable length and diameter.

The results obtained with the rapid test were arbitrarily graded as (1) negative: no oat or sickle cells present; (2) doubtful: 1 or 2 oat cells per oil immersion field and (3) positive: grade 1 when 3 to 5, grade 2 when 5 to 10, grade 3 when more than 10 unmistakable oat cells were present per oil immersion field, grade 4 when several or numerous crescentic erythrocytes were observed per oil immersion field. Interestingly we have not come across a preparation which has to be graded as doubtful or belonging to grade 1. After fifteen minutes' observation time the results of the test are therefore very distinct.

One hundred and sixteen Negroes were examined with the bacteriologic test, and at the same time a control was set up either with the moist stasis method or, when venous blood was used, with an ordinary sealed moist preparation. Of these tests thirty-eight were positive in result. The material selected for these tests comprises ward patients and also patients attending the Hematology Clinic, and the results are therefore not representative for the occurrence of the sickle cell trait in the Negro population of Chicago. Of the 38 patients giving a positive result, 14 had more or less decided sickle cell anemia. This diagnosis was based on the clinical picture, on determinations of the reticulocyte count and the serum bilirubin, on roentgen studies of the bones and on the failure to respond to iron medication. The remainder of the positive reactors, numbering 24, may be classified as belonging to the sickle cell trait group. None of these patients had anemia. With the exception of 1, they were in the hospital for disorders obviously unrelated to the sickling phenomenon. In regard to the exception, a girl aged 6 years with the signs of cerebral thrombosis of unknown origin, the etiologic possibility of the sickling tendency had to be seriously considered. Bauer [8] has emphasized the significance of such manifestations of sickle cell disease.

In only 1 case were the rapid test positive in result and the control entirely negative after forty-eight hours. In 1 out of the 38 cases—i. e. in 2.6 per cent—the rapid test was negative in result after five minutes but positive after fifteen minutes. In no case was the bacteriologic reaction negative and the control positive. The results of our investigations are summarized in tables 1 and 2.

As can be seen from the tables, the rapid test is so sensitive that no differentiation can be made in vitro between the erythrocytes of healthy persons harboring the sickle cell trait and the patients afflicted with sickle cell anemia. This is in accordance with the early observations of Hahn,[3b] who studied the sickle phenomenon with the gas chamber method. Both procedures create the most favorable conditions for the development of the sickling process by rapid reduction of the hemoglobin. Therefore, the variable degree of structural alteration of the red cells which may also contribute to the result is of negligible significance for the bacteriologic test but of far greater importance for the moist stasis test, in which the reduction of oxyhemoglobin takes place much more slowly. The moist stasis test may permit the differentiation between trait and

TABLE 1.—*Sickle Cell Anemia, Fourteen Cases* *

Number of Patients	Rapid Test After		Number of Patients	Control After								
	5 Min.	15 Min.		5 Min.	15 Min.	30 Min.	1 Hr.	2 Hr.	3 Hr.	6 Hr.	24 Hr.	48 Hr.
4	4+	Not determined	1	4+	...	...	...	...	...	...	...	...
9	3+	Not determined	1	0	0	0	4+	...	...	...	...	...
1	2+	4+	2	0	0	0	0	4+	...	...	...	...
			3	0	0	0	0	0	4+	...	...	...
			7	0	0	0	0	0	0	0	4+	...

* Grading scale: 0, negative; 1+, 3 to 5 oat cells; 2+, 5 to 10 oat cells; 3+, more than 10 oat cells; 4+, several or numerous sickle cells per oil immersion field.

TABLE 2.—*Sickle Cell Trait, Twenty-Four Cases* *

Number of Patients	Rapid Test After		Number of Patients	Control After								
	5 Min.	15 Min.		5 Min.	15 Min.	30 Min.	1 Hr.	2 Hr.	3 Hr.	6 Hr.	24 Hr.	48 Hr.
1	4+	Not determined	12	0	0	0	0	0	0	0	4+	...
15	3+	Not determined	8	0	0	0	0	0	0	0	3+	...
4	2+	3+	3	0	0	0	0	0	0	0	0	4+
3	1+	3+	1	0	0	0	0	0	0	0	0	0
1	0	3+										

* An explanation of the grading scale may be found in table 1.

7. Diggs, L. W., and Bibb, J.: The Erythrocyte in Sickle Cell Anemia: Morphology, Size, Hemoglobin Content, Fragility and Sedimentation Rate, J. A. M. A. **112**: 695-700 (Feb. 25) 1939.

8. (*a*) Bauer, J.: Sickle Cell Disease: Pathogenic, Clinical and Therapeutic Considerations, Arch. Surg. **41**: 1344-1362 (Dec.) 1940. (*b*) Bauer, J., and Fisher, L. J.: Sickle Cell Disease with Special Regard to Its Nonanemic Variety, ibid. **47**: 553-563 (Dec.) 1943.

anemia patients so far as relatively rapid sickling is commoner in the latter than in the former condition. However, there is general agreement that the reaction time in the moist stasis test is no indicator of the degree of severity of the anemia. From the clinical point of view it may be emphasized that any positive reaction for the sickling phenomenon should help the physician in the evaluation whether the presenting syndrome may be related to the sickling process. On the other hand, any negative result should permit him to rule out such a consideration. To provide this information as rapidly and as reliably as possible is, therefore, the most essential feature of any satisfactory test for the sickling phenomenon.

MECHANISM OF THE BACTERIOLOGIC TEST

Sickling Phenomenon in Bone Marrow Preparations.—It has already been stated that the mechanism on which the bacteriologic test is based is the rapid reduction of the hemoglobin contained in the corpuscles, which is a necessary requirement for the sickling phenomenon. This explanation is supported by the observation mentioned previously that the effectiveness of the bacterial reagent is directly proportional to the "activity" of the metabolism of the living organisms. The results of the following experiments are also in full accord with this interpretation. 1. If an active culture of B. subtilis is passed through a Seitz filter the filtrate is completely ineffective. 2. If susceptible erythrocytes are suspended in the concentrated white cell layer of centrifuged leukemic blood, sickling occurs as rapidly as with the bacteriologic test. It may be predicted that if a patient harboring the sickling trait should become afflicted with leukemia the moist stasis test would also show rapid sickling. Apparently the respiratory metabolism of the many white cells in such a preparation is equivalent to the oxygen consumption of the bacteria in the rapid test. 3. The same phenomenon can be observed if bone marrow specimens obtained by sternal puncture are examined for their sickling tendencies. Distortion of the red cells occurs much more rapidly than in preparations made with peripheral blood. If the bacteriologic test is used crescent-shaped cells are more numerous in the bone marrow preparation. Hemoglobin-containing nucleated red cells sickle as fast as mature erythrocytes.

Influence of Extracorpuscular Factors on the Sickling Phenomenon.—That the complex sickling cell process may also depend on the presence of certain substances in the plasma has been surmised repeatedly. Several authors[9] have claimed that prolonged washing removes the ability of susceptible red corpuscles to undergo the characteristic distortion, thus indicating the existence and significance of an extracorpuscular mechanism for this peculiar behavior of the erythrocytes. Because the rapid test provides an excellent tool for the study of this problem, we have exposed the red cells of 8 patients belonging to the anemia and the trait group to twenty to forty washings with isotonic solutions of sodium chloride. Afterward these washed cells were placed in the bacterial reagent. Sickling was demonstrable in all these experiments. In 4 out of 8 cases, however, there was an unmistakable prolongation of the reaction time of the rapid test from the usual five minutes to fifteen and even thirty minutes. If the washed red cells used in these delayed reactions were resuspended in normal serum or in plasma obtained from the patients with sickle cell anemia or in bovine albumin, the reaction time reverted to the original value. These results, however, were inconsistent so far as in 4 patients (2 cases of sickle cell trait and 2 of anemia) washing of the red cells had no influence on the results of the bacteriologic test whatsoever. It is, therefore, obvious that the sickling phenomenon does not really depend on an extracorpuscular medium. However, the experiments also show that sometimes a serum factor probably present in the albumin fraction may enhance the sickle cell process.

INDICATIONS FOR THE RAPID BACTERIOLOGIC TEST

Sickle cell disease is a great masquerader.[10] It may simulate many syndromes and if not taken into proper consideration may lead the clinician far astray in his therapeutic activities. The disorder manifests itself as a severe hemolytic anemia; by producing thrombosis in various vascular provinces it may cause bizarre cardiologic, neurologic, dermatologic and acutely surgical syndromes which either accompany the anemia or occur without any severe involvement of the erythropoietic system. Unnecessary operations for ileus, perforated ulcer, acute cholecystitis or appendicitis, for osteomyelitis, confusion with rheumatic fever or tuberculosis are the most common errors met with in clinical practice.[11] On account of these possible diagnostic pitfalls the need for routine examinations for the sickling phenomenon has been emphasized repeatedly.[12] Particularly in the dramatic surgical conditions a rapid test is urgently needed. The presently available methods for the direct demonstration of the sickling process have not been satisfactory, as they do not provide the required information with sufficient rapidity and reliability. Winsor and Burch[13] recently described their diagnostic parameter test in which the influence of sickling on the sedimentation rate of the erythrocyte becomes noticeable. If the sedimentation rates of aerated and of venous stasis blood or of blood saturated with carbon dioxide are compared, a significant retardation in the specimens containing the reduced hemoglobin is indicative of the presence of sickle cell anemia. However, even the parameter test requires more than one hour to deliver decisive result. The great asset of the bacteriologic test is not only the simplicity of the procedure but also the reliability of the negative readings after a reaction time of only fifteen minutes. The recognition of the absence of the sickle cell phenomenon should aid the clinician considerably in reaching a well founded diagnosis. If sickling is present, evaluation of the clinical syndrome should not depend on the laboratory test alone but on the clinical picture as a whole. After all, rheumatic fever or tuberculosis do occur, or the surgical situations mentioned may arise in patients with sicklemia or even sickle cell anemia.

The bacteriologic test may also profitably be employed in the selection of suitable blood donors. As sickle cell

9. Josephs, H. W.: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **40**: 77-84 (Feb.) 1927. Tomlinson, W. J., and Jacob, J. E.: Studies of Sickle-Cell Formation in Normal Saline, Plasma, and Sera with Carbonic Anhydrase Inhibitors, J. Lab. & Clin. Med. **30**: 107-111 (Feb.) 1945.

10. Winsor, T., and Burch, G. E.: Sickle Cell Anemia, "Great Masquerader" Easily Recognizable with Routine Use of Diagnostic Parameter, J. A. M. A. **129**: 793-796 (Nov. 17) 1945.

11. Winsor and Burch.[10] Canby, C. B.; Carpenter, G., and Ellmore, L. F.: Drepanocytosis (Sicklemia) and Apparently Acute Surgical Condition of the Abdomen: Report of Their Occurrence in White Youth with Laparotomy, Arch. Surg. **48**: 123-125 (Feb.) 1944.

12. Bauer and Fisher.[8b] Winsor and Burch.[10]

13. Winsor, T., and Burch, G. E.: Diagnostic Physicochemical Blood Tests in Sickle-Cell Anemia, Am. J. M. Sc. **207**: 152-160 (Feb.) 1944; Rate of Sedimentation of Erythrocytes in Sickle Cell Anemia, Arch. Int. Med. **73**: 41-52 (Jan.) 1944.

anemia is a familial disease and relatives of the patients are commonly used as donors, the advantages of the test are obvious in gaining information whether the prospective donor harbors the trait. Although it is unknown at present whether trait cells have a normal or shortened survival time in the circulation of the anemic recipient, it seems advisable to reject all carriers of the abnormality and to use only normal blood in order to achieve the greatest therapeutic benefit. The same applies to transfusions into nonsickling recipients as long as the conditions which are responsible for the sickling in vivo are only poorly understood. Study of these problems has been recently started in our laboratory by means of the method of cross determinations of the survival time of the erythrocytes.[14] This latter technic employs 2 persons with a compatible blood group simultaneously as donor and recipient (in our study 1 patient with anemia and 1 with sickle cell trait) and by determination of the survival time of the erythrocytes information is obtained whether extracorpuscular or intracorpuscular abnormalities may be present. By means of these experiments, which will be reported elsewhere, it may be possible to shed some light on the etiologic mechanisms in the development of this interesting racial hemolytic syndrome.

SUMMARY

A rapid bacteriologic test for the demonstration of the sickling phenomenon is described. One drop of a turbid broth culture of Bacillus subtilis is mixed with 1 drop of blood, the preparation sealed with paraffin and placed in the incubator at 37 C. Usually after five minutes a positive reaction shows the presence of characteristic oat cells or fully developed sickle cells. If after fifteen minutes no sickling is demonstrable the result can safely be reported as negative.

The mechanism operating in this test is the rapid reduction of the oxyhemoglobin contained in the cells by the respiratory activity of the bacteria. Sickling can only occur if the hemoglobin is present in the reduced state.

The erythrocytes of patients with sickle cell anemia and of healthy persons harboring the sickle cell trait sickle with the same rapidity and to the same extent if the bacteriologic test is employed. In this respect the results of this rapid test differ from the commonly used moist stasis method, in which sickling is often much faster in the group with anemia than in the group with the trait. In the rapid test the development of the sickling process takes place under most favorable conditions. It is directly proportional to the metabolic activity of the bacteria. In the moist stasis test the reaction time depends among other things on the variable number of cells having an oxygen consumption, namely, white cells, reticulocytes and nucleated red cells. These are more numerous in the group with anemia.

If susceptible red cells are suspended in the white cell layer of centrifuged leukemia blood sickling occurs as rapidly as with the bacteriologic test. In preparations of bone marrow sickling takes place much more rapidly than in preparations with peripheral blood. When the bacteriologic test is used hemoglobin-containing nucleated red cells sickle as fast as mature erythrocytes.

Repeated washings of the cells with saline solution does not abolish the sickling phenomenon. However, the reaction time of the rapid test is sometimes prolonged by this treatment of the erythrocytes. Restoration to a normal reaction time can be achieved by the resuspension of the cells in serum or in bovine albumin.

The rapid test should be employed as a routine test for all Negro patients.

The rapid test is of great advantage in the selection of blood donors. Blood of carriers of the sickle cell trait should not be used for transfusions, as it is unknown at present whether trait cells have a normal or shortened survival time in the circulation of the anemic recipient and it seems to be advisable to use only normal blood in order to achieve the greatest therapeutic benefit.

Addendum: Since this paper was submitted determinations of the survival time of "trait" cells transfused into patients with sickle cell anemia were performed. In 3 instances the "trait" cells survived normally, that is, about 100 to 120 days. On the basis of these experiments it seems permissible to use "trait" cells for therapeutic blood transfusions.

14. Singer, K.: Problems of Erythrocyte Disintegration with Particular Reference to the Life Span of the Red Cell, J. Lab. & Clin. Med. **30**: 784-799 (Sept.) 1945.

DIURETICS

ARTHUR C. DeGRAFF M.D.
New York

Mercurial diuretics now form a necessary part in the treatment of congestive heart failure. This is particularly true in the case of those patients who no longer show any response to digitalis therapy. Attention should be called to the fact that mercurial diuretics act on the tubules of the kidney interfering there with the reabsorption of water and sodium chloride. The effect on the heart is, therefore, secondary. The fall in venous pressure may not occur for several hours after diuresis has begun from the intravenous injection of a mercurial, whereas the venous pressure begins to fall within ten minutes after the intravenous administration of a rapidly acting glycoside such as ouabain.

All three of the commonly used mercurial diuretics in this country contain theophylline. In mercurophylline injection ("mercuzanthin") the theophylline is in molar equivalent amounts with the mercurial compound. In mersalyl and theophylline ("salyrgan-theophylline") and in meralluride sodium solution ("mercuhydrin") the theophylline is in excess. The presence of theophylline prevents necrosis of tissues at the site of injection, increases the rate of absorption from the site of an intramuscular injection, prevents the storage of mercury and increases the concentration of the mercurial within the kidney, thus contributing to a greater diuretic response.

The formulas of the three commonly used mercurial diuretics are as follows:

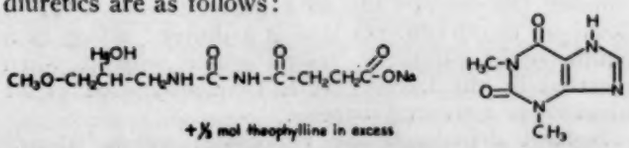

Fig. 1.—Meralluride sodium solution.

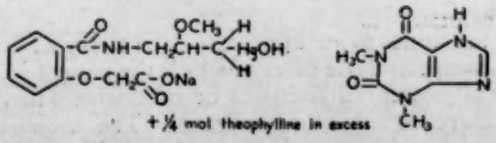

Fig. 2.—Mersalyl and theophylline.

Read in a panel discussion on The Modern Management of Heart Disease in the General Scientific Meetings at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1947.

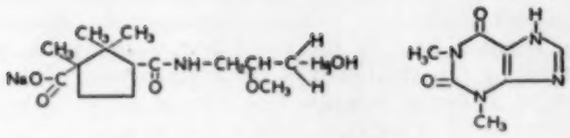

Fig. 3.—Mercurophylline.

All three mercurials have about the same degree of effectiveness. When they are given intravenously diuresis begins in about half an hour and reaches its peak within four hours. The amount of diuresis varies considerably from patient to patient and even in the same patient from time to time. However, if there is any edema fluid at all, one can anticipate some diuresis in well over 90 per cent of patients when the drug is given either intravenously or intramuscularly. When the patient has dehydration symptoms from rapid diuresis, it is probably better to give small doses of the diuretic more frequently rather than one large dose, such as 2 cc., once a week, for instance. Doses larger than 2 cc. should never be given. The intramuscular route is probably safer than the intravenous route.

A diuresis can be obtained in about 70 per cent of patients by the use of a suppository of either mersalyl and theophylline or "mercuzanthin." Rectal irritation may occur so that special care must be taken in the use of this dosage form.

The oral administration in the form of tablets is quite satisfactory in about 60 per cent of patients who have a moderate degree of congestive heart failure. A tablet may be given once or twice a day, preferably after a meal to avoid gastric irritation. Tablets of mersalyl and theophylline and of mercurophylline are available. In many cases by the judicious combination of the oral and parenteral dosage forms it is possible to give the injections much less frequently.

Morphine, meperidine hydrochloride and possibly other hypnotics or sedatives can exert an antidiuretic effect. It is important, then, if an adequate diuresis is not obtained with a mercurial diuretic to be sure that the patient is not receiving one of these drugs at the time.

Enhancement of mercurial diuresis can be produced by administration of ammonium chloride in doses of 3 Gm. a day. The diuresis may increase as much as 20 per cent if the ammonium chloride is administered for two or three days before the diuretic is given. Ammonium nitrate and potassium chloride will also enhance the diuresis but to a lesser extent. Urea in doses up to 60 Gm. per day is a diuretic acting as a nonthreshold substance, taking water with it when excreted by the kidney. It is frequently used as an adjuvant to mercurial diuresis.

Sodium dehydrocholate ("decholin sodium") will also enhance the effect of a mercurial diuretic. It can be given intravenously at the same time the diuretic is given.

The xanthines alone are rarely used today as diuretic agents except in those cases in which the patient is sensitive to all mercurial diuretics or otherwise when mercurial diuretics are contraindicated. Theobromine and sodium salicylate, theophylline, theophylline ethylenediamine and "theocalcin" are all of about equal effectiveness as diuretic agents. Diuresis, however, is not nearly as complete or uniform as when the mercurials are used.

The mercurial diuretics are not entirely free from danger, and care must be taken to observe danger signals while patients are receiving the treatment. Among the reactions which may be noted are: 1. Sensitization to one of the mercurials. This is manifested as urticaria, rash, chills and fever, sense of tightness in the chest, etc. If any signs of sensitization appear, one of the other mercurials should be substituted. All three diuretics have been reported as causing reactions in susceptible patients. 2. Digitalis toxicity. Spontaneous redigitalization even to the point of toxicity by mobilization of digitalis from edema fluid may occur. This may be avoided by giving the diuretic in smaller amounts or having the patient initially on a smaller digitalis maintenance dose. 3. Depletion of sodium. This may occur with muscle cramps, abdominal colic, nausea and vomiting, especially in patients on a low sodium diet. 4. Sudden death. This is relatively rare, considering the extensive use of these agents and the fact that they are used in many terminal cases. However, the incidence of sudden death can be reduced if care is taken not to give a diuretic that has caused a reaction previously and to avoid giving this medication to patients with advanced renal or hepatic disease.

ABSTRACT OF DISCUSSION

VALUE OF OXYGEN

QUESTION: When can oxygen help patients with cardiac disease?

ANSWER: Oxygen is of value to any patient with cardiac disease who shows signs of arterial oxygen unsaturation. This is usually manifested by the presence of cyanosis. It should be pointed out, however, that cyanosis which is due to a shunt from the venous side to the arterial side, such as in congenital heart disease, or cyanosis related to definite stagnation of blood in the peripheral vessels is not helped by oxygen. Cyanosis in which there is arterial unsaturation due primarily to some disturbance in ventilation such as pulmonary congestion or pulmonary edema is definitely benefited by oxygen. Such conditions would occur in coronary artery thrombosis and in acute failure of the left ventricle.

AMMONIUM CHLORIDE AS DIURETIC

QUESTION: How important is ammonium chloride as a diuretic per se?

ANSWER: Ammonium chloride alone is a mild diuretic. It serves an important purpose to substitute the ammonium radical for sodium. It is valuable as an adjuvant to a mercurial diuretic; the diuresis is increased by about 20 per cent when up to 3 Gm. of ammonium chloride is given per day.

SALICYLATES FOR RHEUMATIC FEVER

QUESTION: Do the salicylates cure rheumatic fever?

ANSWER: Salicylates will relieve the articular symptoms of rheumatic fever, reduce the fever and make the patient much more comfortable. There is serious doubt, however, whether they influence in any way the course of the disease. Although salicylates have been given in large doses within recent years, the large doses are not free from danger. It should be emphasized that salicylate poisoning can occur and even death may result from an overdosage of salicylates.

UREA AS DIURETIC

QUESTION: How effective is urea as a diuretic?

ANSWER: Urea as a diuretic has about the same effectiveness as ammonium chloride. It must be given in large doses.

COMPRESSION OF LIMBS AND VENESECTION

QUESTION: What is the place of compression of the limbs and venesection in heart disease?

ANSWER: Rapid removal of blood from veins does relieve the load on the right side of the heart in acute heart failure. It is not generally a good plan to use this technic, particularly if the patient has anemia. As an emergency measure it has a limited value. It is possible by compression of the veins on all four extremities to pool a fairly large portion of the circulating

blood in the extremities and thus relieve the load on the heart.

USE OF EPINEPHRINE IN CARDIAC ASTHMA

QUESTION: What is the value of epinephrine in cardiac asthma?

ANSWER: Cardiac asthma is another term for failure of the left ventricle of the heart and occurs in hypertensive heart disease, aortic insufficiency, aortic stenosis and, occasionally, coronary artery thrombosis. It is an indication of the inability of the left ventricle to pump out the blood that is received by it. Epinephrine is not a particularly safe drug to use in such conditions because of the fact that it may cause a sudden rise in blood pressure. However, in small doses it does decrease the bronchial spasm which is associated with failure of the left ventricle and may give relief. It is probably better to give an intravenous injection of a rapidly acting glycoside such as ouabain and to administer oxygen by inhalation or to give aminophylline very slowly intravenously. Attacks of cardiac asthma can be prevented by a maintenance dose of digitalis or by the use of mercurial diuretics.

DIGITALIS

HARRY GOLD, M.D.
New York

The intensive search for purified glycosides of the digitalis series in the past seventy-five or eighty years has resulted in the discovery of numerous principles or mixtures of principles such as "digifolin," "digalen," "urginin," "digilanid," lanatoside C ("cedilanid"), digoxin, ouabain, strophanthin and digitoxin ("digitaline Nativelle"). The extent of absorption from the gastrointestinal tract constitutes the most important point of difference between these materials from the practical standpoint, and with respect to this point the vast majority of the purified materials offer no advantage over the whole digitalis leaf. Digitalis leaf has therefore continued to maintain its position of preeminence among the cardiac glycosides in common use. A satisfactory index of absorption in man may be obtained by the ratio of the oral to the intravenous dose necessary to produce the same effect in patients with auricular fibrillation. If this ratio is 10:1, 10 per cent is absorbed; if the ratio is 5:1, 20 per cent is absorbed, and if the ratio is 1:1, 100 per cent is absorbed. For instance, in the case of a preparation of convallaria, 80 units by mouth were found to produce less effect than 3 units by vein; about 3 per cent was absorbed. An experiment showing the average behavior of 12 patients with auricular fibrillation who received 1.2 mg. of digitoxin, one time by mouth and at another time by vein, shows that in the case of this drug the ratio is 1:1. This means that practically 100 per cent of an oral dose is absorbed. It was found that in order to produce the same effect in the same person, it requires 40 units of lanatoside C, 20 units of digitalis and only 4 units of digitoxin. Since digitoxin is all absorbed, it follows that only 20 per cent of the active material in digitalis is absorbed, and only 10 per cent of a dose of lanatoside C is absorbed. A comparison was made of digitalis and digitoxin. Patients with auricular fibrillation received 1.2 mg. of digitoxin at one time. The curve showing the development and the disappearance of the action was drawn. After the effects wore off, the same patients received 1.2 Gm. of digitalis at one time. The two curves are identical, showing that digitoxin acts like digitalis leaf when given by mouth, with respect to the speed of absorption and speed of elimination. The difference lies in their potency; digitoxin is approximately a thousand times as potent as the standard digitalis leaf of the present "Pharmacopoeia." Where one would use 1.2 Gm. of digitalis, one may obtain the same effect by using 1.2 mg. of digitoxin.

Because of the high potency of digitoxin, I have advocated the use of the average full digitalizing dose to be given at one time to patients with heart failure who have not recently had digitalis. This produces the full effects in six to ten hours, instead of the thirty-six to seventy-two hours as in the case of the divided dose method using digitalis leaf. Digitalis leaf cannot be used that way because the large quantity of non-absorbable glycosides in the leaf cause vomiting by local action in 1 of every 5 patients.

Experience with this single digitalizing dose of digitoxin shows that 1.2 mg. given at one time may be expected to reduce the apex rate in patients with auricular fibrillation to between 60 and 85 a minute in about three fourths of the patients. This may be regarded as satisfactory digitalization. Some of the rest of the patients could do with somewhat less or require more to complete the digitalization.

The daily maintenance dose is usually 0.2 mg. In a few patients, the dose needs to be reduced to 0.1 mg., and some of the more tolerant patients require as high as 0.3 mg. or more daily.

The use of digitoxin has greatly simplified the problem of digitalization. I advocate it as the material of choice for routine oral digitalization and maintenance. There are reasons for the belief that it will not be long before the crude digitalis leaf or the tincture will be a cardiac medication of historical interest chiefly, and that digitoxin will take its place.

Read in a panel discussion on The Modern Management of Heart Disease in the General Scientific Meetings at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1947.

ABSTRACT OF DISCUSSION

VALUE OF AMINOPHYLLINE

QUESTION: Of what value is aminophylline (theophylline ethylenediamine) in coronary or other types of heart disease?

ANSWER: I do not believe that aminophylline has any value in the routine treatment of the angina of effort by oral administration. I know that it is widely used for that purpose, but in a study which we made some years ago by means of the "blind test" we found that patients were unable to distinguish aminophylline from sugar of milk tablets in relation to the control of cardiac pain on effort. There is no doubt that an intravenous injection of 0.24 Gm. of aminophylline will dilate the coronary vessels, and it may be of some use in acute coronary thrombosis. There are some who use it routinely after coronary thrombosis with a view to making patients less susceptible to ventricular fibrillation and reducing the size of the final scar. I do not use it that way. I am not impressed with the evidence that it produces those results. Furthermore, if I find it necessary to use a coronary vasodilator in coronary thrombosis, I give glyceryl trinitrate under the tongue at frequent intervals. It is more effective than aminophylline for that purpose. There is, of course, the problem of pulmonary edema with bronchospastic symptoms in coronary thrombosis, and in such cases an intravenous dose of aminophylline is often rather helpful. As a diuretic in congestive failure, which sometimes occurs in coronary artery disease, aminophylline is effective but not nearly so effective as the mercurial diuretics.

ALLERGY TO DIGITALIS

QUESTION: Is there any allergy to digitalis?

ANSWER: I have never seen any cases of allergy to digitalis. Several years ago a few cases of allergic reactions to digitalis were reported. It must be rare if it occurs at all.

USE OF DIGITALIS TO PREVENT HEART FAILURE

QUESTION: Can digitalis be used to prevent heart failure or delay its onset or to check cardiac enlargement?

ANSWER: This question requires some dissection. There is no doubt that the maintenance dose of digitalis prevents the recurrence of heart failure, and theoretically its use before heart failure occurs might delay its onset or prevent failure. If one were to take a suggestion from this, one might begin the use of digitalis in a patient with cardiac disease long before failure is in evidence. It would mean keeping all patients with heart disease under the influence of digitalis for the rest of their life, for all patients with heart disease are candidates for failure. I do not pursue this practice. I am not certain whether I am right or wrong. I might mention that there is the view that cardiac enlargement is a manifestation of a failing muscle and that keeping the muscle under the influence of digitalis might retard enlargement. This is a point that cannot be easily proved.

EXPENSE OF DIGITALIS GLYCOSIDES

QUESTION: What is the expense of the digitalis glycosides in contrast to the dried leaf? Is such expense only a temporary drawback?

ANSWER: I do not know the relative costs of the various purified glycosides as compared with the ordinary dried leaf. In relation to digitoxin, which I believe should replace the crude leaf for routine oral administration, I was recently informed that the cost of the glycoside has been greatly reduced, and that a dose of digitoxin now costs the patients about the same as an equivalent dose of digitalis leaf.

NOTE BY DR. PAUL D. WHITE: In one of the large drugstores in Boston the following prices of digitalis preparations were quoted:

Trade Name	Source	Strength of Tablet	No. of Tablets	Retail Price at Pharmacy
Digitoxin	Abbott	0.20 mg.	100	$1.85
Digitaline Nativelle	Fougera	0.20 mg.	100	3.00
Digitoxin	Squibb	0.20 mg.	100	1.85
Purodigin	Wyeth	0.20 mg.	100	1.85
Digoxin	Burroughs Wellcome	0.25 mg.	100	2.25
Cedilanid	Sandoz	0.50 mg.	100	4.00
Digilanid	Sandoz	0.50 mg.	100	3.00
Digiglusin	Lilly	0.1 Gm. (1½ gr.)	100	1.25
Digalen	Roche	0.1 Gm. (1½ gr.)	100	2.25
Dried leaf				
Digifoline	Ciba	0.1 Gm. (1½ gr.)	100	3.00
Digitalis	Davies, Rose	0.1 Gm. (1½ gr.)	100	2.20
Digitalis	Lederle	0.1 Gm. (1½ gr.)	100	1.07
Digifortis	Parke Davis	0.1 Gm. (1½ gr.)	100	2.15
Digitos	Sharp & Dohme	0.1 Gm. (1½ gr.)	100	1.25
Digitalis	Squibb	0.1 Gm. (1½ gr.)	100	1.25
Digitora	Upjohn	0.081 Gm. (1.28 gr.)	100	0.53

TOXICITY OF DIGITALIS LEAF

QUESTION: Is digitalis leaf more toxic than the glycosides when equally effective?

ANSWER: No. Whatever evidence there is on the subject shows that the spread between the therapeutic and toxic doses of digitoxin is the same as for digitalis leaf. It must be remembered, of course, that the potency of digitoxin is about 1,000 times that of digitalis and that one should prescribe 0.1 mg. of digitoxin where one would otherwise prescribe 0.1 Gm. of digitalis.

The Circulatory System.—Arterial functions are controlled directly by peripheral centers, probably intramural. These are under a double dynamogenic influence: (*a*) that of the central nervous system (centers of the spinal cord and of the medulla); and (*b*) that of the cardiac sinus. This latter structure is able to induce either paralysis or tonic rigidity of the arteries, conditions which can be modified only by an extremely violent stimulation of the nerve centers as that which occurs with their destruction. The circulatory system has a complex regulatory mechanism which is influenced by the nervous system but has in itself the means of self-regulation.—Marceau, F.: Physiological Properties of Arteries, *Experimental Medicine and Surgery*, February, 1948.

QUINIDINE

LOUIS N. KATZ, M.D.
Chicago

There is a remarkable similarity in the discovery of the utility of quinidine with that of digitalis in that both were made by laymen. In 1914 one of Wenckebach's[1] patients informed him that the quinine which he had prescribed for malaria made his irregular heart action (due to auricular fibrillation) regular. Wenckebach was quick to find that quinine was an effective drug in the treatment of auricular fibrillation. Frey,[2] in 1918, established the fact that quinidine, a closely related compound, was more effective for this purpose. This was soon confirmed and extended by many workers, notably by Sir Thomas Lewis.[3] However, the early enthusiasm for quinidine soon waned because of a number of unexpected deaths attributed to it, and the pendulum swung back to nearly complete abandonment of the drug. Recently, as experience in its use improved, it has come to play an important role in cardiac therapy.

Its recent use has been increased in part because of the growing realization that large doses may be used with relative safety as well as because of the establishment of its effectiveness in ventricular tachycardia and in cases of coronary disease with premature systoles. Its utility in converting auricular fibrillation to sinus rhythm has long been established.

In this presentation a summary will be given of the present status of quinidine in cardiac therapy with some notes on the most recent developments.

It is now established[4] that quinidine prolongs the refractory period of the heart and the electrical systole of the ventricles. It prolongs conduction in the ventricles, in the auriculoventricular junction and, to a certain extent, in the auricles. It decreases the excitability of the myocardium and acts as a "soothing agent" on ectopic pacemakers. It depresses the sinus node and tends thereby to slow the heart rate. It paralyzes the action of the vagus nerve, which tends to neutralize to a certain extent its direct effects particularly on the sinus node and auricles. So far as it leads to a slowing of the heart rate it causes an increased amplitude of contraction, since more time is available for filling of the heart. In excess, however, it is a poison which tends to depress the myocardium and may lead to respiratory disturbances and even respiratory arrest. By virtue of its direct action on the smooth muscles of the blood vessels it may, with large doses, cause a fall in blood pressure. These multiple actions of quinidine explain the fact that contrary effects on certain properties of the heart may develop.

Quinidine has definite effects on the electrocardiogram.[5] It alters the P wave and the QRS complex.

From the Cardiovascular Department, Michael Reese Hospital. The department is supported in part by the Michael Reese Research Foundation.
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1. Wenckebach, K. E.: Die Unregelmässige Herztätigkeit und ihre Klinische Bedeutung, Leipzig, W. Engelmann, 1914.
2. Frey, W.: Weitere Erfahrungen mit Chinidin bei Absoluten Herzunregelmässigkeit, Klin. Wchnschr. **55**: 849, 1918.
3. Lewis, T.; Drury, A. N.; Wedd, A. M., and Iliescu, C. C.: Value of Quinidine in Cases of Auricular Fibrillation and Method of Studying Clinical Reaction, Am. J. M. Sc. **163**: 781, 1922.
4. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.
5. Katz, L. N.: Electrocardiography, ed. 2, Philadelphia, Lea & Febiger, 1946.

It prolongs QRS duration, leading to intraventricular block. It prolongs the P-R interval and may lead to more advanced auriculoventricular block. It may cause sinoauricular block. It leads to deviations of the S-T segment and may greatly alter the T wave, inverting it, notching it and prolonging its duration. It may lead to ectopic rhythms of various sorts. Particularly hazardous is the appearance, with excessive doses, of ventricular premature systoles, tachycardia and fibrillation.

Quinidine is rapidly absorbed and excreted. With the oral route, its maximum effect is obtained in two to four hours. This has been demonstrated indirectly by its effect on the auricular rate in auricular fibrillation, its effect on the duration of electrical systole and directly by chemical analysis of the blood.[6] With intramuscular or intravenous administration, the maximum effect occurs sooner, in one-half to one and one-half hours. With the oral route, minimal residual effects persist for six to eight hours, and the effect is completely gone and no further urinary excretion occurs in twelve to twenty-four hours. When repeated doses are given the effects of each are additive. The clinical implications from these data are: (1) that repeated oral doses given more than six hours apart are not cumulative; (2) that the interval between doses should be less than six hours and preferably two to four hours, and (3) that cumulation may occur when the drug is administered every hour or two.

One of the important considerations of quinidine is its toxicity.[7] This may be the result of idiosyncrasy with the symptoms of cinchonism. While this is rare, it is safest to employ a test dose of 0.2 Gm. by mouth and wait two to three hours for reaction before proceeding further. Cinchonism may also develop during therapy with larger doses of quinidine. The evidence of this intoxication includes tinnitus, vertigo, visual disturbances, nausea, vomiting, diarrhea, headache, confusion, syncope, fever, cutaneous rashes, petechiae and angioneurotic edema. More serious than these are the respiratory disturbances such as asthma, depression of breathing and even respiratory arrest. A troublesome finding in its use in auricular fibrillation or flutter is the paradoxic tachycardia which may follow the slowing of the auricular rate. For this reason some clinicians prefer to depress auriculoventricular conduction with digitalis in such cases before or simultaneously with quinidine. A serious hazard is the development of ventricular fibrillation or cardiac asystole. The danger of the occurrence of embolism when auricular fibrillation is converted to sinus rhythm must be considered. However careful studies show that this does not occur as often as suspected. Many of the episodes attributed to embolism are really because the direct effect on the heart leads to asystole or ventricular fibrillation. It is stated that the occurrence of petechiae is to be considered a warning sign of impending embolization.

INDICATIONS FOR USE OF QUINIDINE

The indications for the use of quinidine are at least seven in number:

1. Quinidine is an effective drug in breaking the mechanism of paroxysmal tachycardia of supraventricular origin. It has been widely employed for this purpose with excellent results.

2. Quinidine has been effectively employed to break the mechanism of paroxysmal ventricular tachycardia, chaotic heart action and, on occasion, even paroxysmal ventricular fibrillation. These mechanisms are so detrimental to the heart, especially when complicated by organic heart disease, that quinidine has been a blessing under such circumstances. Papaverine has been employed for similar purposes.[8]

3. Quinidine has been employed prophylactically to prevent recurrent paroxysmal arrhythmias. It has proved to be as valuable prophylactically as in breaking the mechanism of these forms of rapid heart action.

4. One of the newer developments in the use of quinidine is its employment to suppress frequent premature systoles. In normal subjects this should be employed only when the premature systoles cause distressing symptoms. For example, I have recommended its use by a surgeon who during operation experienced frequent premature systoles which were subjectively very disturbing whenever he ran into unexpected difficulties. It proved effective. There is no need to stress the fact that premature systoles without symptoms occurring in normal persons require no therapy, and care should be taken not to give cause for "cardiac fixation" in such subjects by suggestion of therapy. Quinidine may be used when digitalis causes premature systoles. Of course, under these circumstances digitalis should be stopped or the dose diminished. However, the use of quinidine will tend to lessen such digitalis-engendered premature systoles, especially when the benefits of digitalis require a dose which leads to ectopic beats. Quinidine may be used prophylactically in patients with mitral stenosis complicated by frequent auricular premature systoles in order to prevent or delay the onset of auricular fibrillation.

However, the most important use of quinidine in the case of premature systoles is the suppression of ventricular premature systoles in patients with coronary disease, whether this be an acute infarction or a variety of chronic coronary insufficiency. By "soothing" the ectopic pacemaker quinidine tends to avoid the risks of the development of paroxysmal tachycardia and the more serious ventricular fibrillation, which may cause unexpected death. In the presence of ventricular premature systoles in coronary disease quinidine is one of the important and potent forms of therapy. Some have gone so far as to employ quinidine in all cases of recent infarction. Quinidine will definitely lessen deaths in coronary disease attributed to ventricular fibrillation. In chronic coronary insufficiency it will lessen the frequency of congestive failure and angina pectoris, both of which may be precipitated by frequent premature systoles. Under these circumstances quinidine is one of the potent drugs available in prophylaxis of angina pectoris and heart failure.

5. Recently[9] it has been shown that quinidine in large doses will abolish, in most cases, the mechanism of the Wolff-Parkinson-White syndrome. This is used diagnostically and not therapeutically.

6. (*a*) Sagall, E. L.; Horn, C. D., and Riseman, J. E. F.: Studies on the Action of Quinidine in Man: I. Measurement of the Speed and Duration of the Effect Following Oral and Intramuscular Administration, Arch. Int. Med. **71**: 460 (April) 1943. (*b*) Sturnick, M. I.; Riseman, J. E. F., and Sagall, E. L.: Studies on the Action of Quinidine in Man: II. Intramuscular Administration of a Soluble Preparation of Quinidine in the Treatment of Acute Cardiac Arrhythmias, J. A. M. A. **121**: 917 (March 20) 1943. (*c*) Delevett, A. F., and Poindexter, C. A.: Plasma Concentrations of Quinidine with Particular Reference to Therapeutically Effective Levels in Two Cases of Paroxysmal Nodal Tachycardia, Am. Heart J. **32**: 697, 1946.

7. Goodman and Gilman,[1] Carter, J. B.: Use and Abuse of Quinidine, M. Clin. North America **29**: 215, 1945.

8. Lindner, E., and Katz, L. N.: Papaverine Hydrochloride and Ventricular Fibrillation, Am. J. Physiol. **133**: 155, 1941.

9. Littman, D., and Tarnower, H.: Wolff-Parkinson-White Syndrome: A Clinical Study with Report of Nine Cases, Am. Heart J. **32**: 100, 1946.

6. Quinidine is useful in converting auricular fibrillation to a sinus rhythm. This is especially true of paroxysmal auricular fibrillation, but the drug may be of value in more persistent auricular fibrillation with minimal heart disease and little cardiac enlargement and of less than six months' duration. The question always arises whether digitalis may be preferred to keep the ventricular rate slow in view of the tendency of the auricular fibrillation to recur in many patients with chronic heart disease. However, when the converted sinus rhythm is supported by prophylactic quinidine therapy the risk of recurrence is reduced or at least put off for long periods of time. Recently [10] the use of quinidine has been advocated in longer-standing auricular fibrillation with more advanced heart disease and cardiac enlargement, particularly in patients with rheumatic heart disease accompanied by frequent emboli. It is hoped by such therapy to prevent the occurrence of a fatal embolism. However, the use of quinidine here is hazardous, and the clinician must weigh the risk of quinidine toxicity against the chance of a fatal embolism. It may be employed after thyroidectomy to convert a persisting auricular fibrillation to sinus rhythm. It may be used cautiously in patients with recent myocardial infarction to convert recent auricular fibrillation to sinus rhythm. Under these circumstances only the smaller doses should be employed, since the risk of further depressing a depressed heart makes its use a heroic procedure. The preliminary (or simultaneous) use of digitalis to prevent paradoxic tachycardia should be considered, particularly since rapidly acting digitalis may, on occasion, itself convert the rhythm. Quinidine does not convert all cases of auricular fibrillation. The usual experience is that it is effective in about 50 per cent of cases, and of these about one half recur.

7. Quinidine has been used to convert auricular flutter to sinus rhythm. It is less effective in flutter than in fibrillation, and digitalis is ordinarily preferable. Quinidine may be used in auricular flutter after digitalis has converted the flutter to fibrillation without leading to sinus rhythm. Quinidine may convert such an auricular fibrillation to sinus rhythm.

The only absolute contraindication to the use of quinidine is idiosyncracy or sensitivity to the drug. This is manifested by cinchonism or by respiratory or circulatory collapse. Sometimes the toxic action of the drug in patients who are sensitive to it may appear before its therapeutic effects occur. Obviously under such circumstances the drug is contraindicated. Most of the contraindications are relative and are based on the primary depressant action which quinidine has on the heart. Thus it is contraindicated ordinarily in acute infections and subacute bacterial endocarditis, presumably because of the hazards that quinidine will add to the depression of the already diseased heart. It is not very effective in long-standing auricular fibrillation.

Another relative contraindication to the use of quinidine is the presence of pronounced cardiac enlargement, long-standing heart disease or congestive failure, particularly when considering conversion of auricular fibrillation to sinus rhythm. It is in such cases that the depressant action of quinidine on the heart is most apt to appear. Intraventricular block or auriculoventricular block is a relative contraindication to the use of quinidine unless frequent premature systoles are also present. The presence of block is a sign of an already depressed myocardium to which the depressant action of quinidine may be added. While some clinicians fear the preoperative use of quinidine in patients with hyperthyroidism and auricular fibrillation because of frequent recurrence of the arrhythmia after operations, I feel that this danger may be obviated by the continuance of quinidine in prophylactic doses during the postoperative period

METHODS OF ADMINISTRATION

Quinidine may be administered orally, intramuscularly or intravenously.

The oral route is the most satisfactory in the majority of cases. In every instance a test dose of 0.2 Gm. should be given and the patient followed closely for reaction for several hours before proceeding further. Although unpleasant side actions are rare, it is wisest to carry out this preliminary procedure. For therapeutic effect, 0.4 Gm. should be given every two hours until the arrhythmia is broken or until five doses have been given. This may be repeated for two or three days, the dose being increased each day by 0.2 Gm. Administration of quinidine should be stopped when toxic symptoms appear. In all cases the patient should be under close observation.

When the arrhythmia is broken, 0.2 Gm. of quinidine should be given three times a day for one week. If the arrhythmia is recurrent maintenance therapy, 0.2 Gm. two or three times a day, should be employed; otherwise quinidine should be discontinued. When maintenance doses are used there is no need for the close observation employed with the larger doses, but the patient should be seen frequently by the physician.

Actually, the dosage is variable from case to case. It is probably safe to give up to 4 Gm. a day. As much as 8 Gm. in twenty-four hours, 12.5 Gm. in two and one-half days and 35 Gm. in nine days have been given.[11] As much as 1 Gm. has been given as a single dose, but this is rarely used. It must be stressed that whenever intensive quinidine therapy is employed the patient should be in the hospital and under constant observation. The patient should be observed and the apical heart rate determined before each dose, therapeutic and toxic effects being watched for.

The drug should be discontinued: (1) when the rhythm has been returned to normal; (2) when a significant increase in heart rate occurs (thus in auricular fibrillation when the rate goes over 140 per minute), or (3) when intraventricular block occurs, as this is supposed to be a danger sign of ventricular fibrillation. It is stated that quinidine should be discontinued when petechiae appear, as this is taken to indicate imminent embolism. The occurrence of cinchonism demands immediate withdrawal of the drug.

Intramuscular therapy is indicated when more rapid action is needed; that is, an action in one-half to one and one-half hours, or when oral administration is not feasible. Quinidine sulfate or quinidine hydrochloride may be used. Recently it has been suggested that quinidine may be made soluble by combining it with urea and antipyrine. The dosage schedule is similar to that outlined in the oral method. Intramuscular quinidine should be given under close observation in the hospital. On occasion, quinine dihydrochloride has

10. White, P. D., and Blumgart, H.: Cessation of Repeated Pulmonary Infarction and of Congestive Failure After Termination of Auricular Fibrillation by Quinidine Therapy, J. Mt. Sinai Hosp. **8**: 1093, 1942.

11. Zimmerman, S. L.: Ventricular Tachycardia: A Report of Ten Cases, Eight of Which Were Treated with Quinidine with Recovery in Seven, Ann. Int. Med. **23**: 634, 1945.

been found to be effective intramuscularly.

The intravenous route is rarely necessary and is dangerous. It is to be used only when ventricular tachycardia has precipitated pulmonary edema or severe congestive failure. Very close observation of the patient is necessary and the drug must be stopped at once as soon as the therapeutic effect is noted or toxic symptoms appear. Caffeine and sodium benzoate should be at hand (0.5 Gm. intravenously or intramuscularly) to counteract respiratory failure, the fall in blood pressure or other collapse reactions. Even so, quinidine has led to the death of patients when given intravenously. It is heroic therapy and should be recognized as such. For intravenous administration 0.2 to 0.4 Gm. of quinidine may be dissolved in 10 cc. of water and given extremely slowly. It is preferable, however, to dissolve 4 Gm. in 500 cc. of a 5 per cent solution of dextrose and water and to administer it in a constant drip at the rate of about 10 drops per minute.

Quinidine has no true pharmacologic antidote. The drug of choice to counteract respiratory depression is caffeine and sodium benzoate. "Metrazol" (pentamethylenetetrazol), amphetamine, nikethamide and picrotoxin are effective, but may themselves aggravate the respiratory depression if large doses of quinidine have been used.[12] The most potent circulatory stimulants to neutralize the fall in blood pressure are "paredrine" (2-[2-methylaminopropyl]-phenol) and phenylephrine hydrochloride. Desoxyephedrine, epinephrine and amphetamine may also prove of value.

Recently[4c] the determination of plasma quinidine levels has been employed in the course of treatment. It was found that when the plasma levels exceeded 1 mg. per liter bouts of paroxysmal tachycardia were eliminated, only to recur when the levels fell below 1 mg. per liter. The utilization of blood levels may lead to a more quantitative and rational approach to quinidine therapy in the future.

DIHYDROQUINIDINE AND FAGARINE

The early work of Lewis showed that dihydroquinidine, an alkaloid present in commercial quinidine, to the extent of about 20 per cent, was more effective than quinidine in human auricular fibrillation. It has recently been shown[13] that dihydroquinidine is also more effective in protecting animals against experimental ventricular fibrillation. The relative effectiveness of quinidine and dihydroquinidine in human auricular fibrillation was reinvestigated during the war by a committee working under the auspices of the National Research Council, and the early work of Lewis was confirmed.[13a]

From the Argentine there has come a report[14] that fagarine, an alkaloid obtained from trees growing in that country, could be used as a possible substitute for quinidine. Like quinidine this drug has a depressant action on the cardiac properties of the heart of amphibia, rabbits and dogs. It was more effective than quinidine in raising the threshold for auricular and ventricular fibrillation to faradic stimulation, and it abolished spontaneous auricular fibrillation in these animals. Taquini has used it in patients with auricular flutter and fibrillation. Within thirty minutes, in all 6 cases, normal sinus rhythm was instituted after a single dose of fagarine (0.06 to 0.1 Gm. of fagarine hydrochloride intramuscularly). In 1 case in which auricular flutter recurred after twenty-eight days, fagarine again restored sinus rhythm. Unfortunately this drug has not been available in the United States, but if further work by other investigators confirms the studies of the South American group, a new drug can be added to our armamentarium.

SUMMARY

In the course of the years following its introduction quinidine has obtained a definite and secure place in the treatment of heart disease. When properly used with due precautions, the results are brilliant.

The criteria for its use can be summarized in the words of the National Research Council[15] as being:

1. Ventricular tachycardia diagnosed electrocardiographically.
2. Congestive heart failure that appears definitely to have been precipitated by the sudden onset of auricular fibrillation (if not adequately controlled by digitalis).
3. Persistent premature ventricular contractions in patients who have had acute coronary artery occlusion.
4. Chronic disease of the heart associated with paroxysmal auricular fibrillation, paroysmal auricular tachycardia or auricular flutter.
5. A history of systemic embolization in a case of paroxysmal or established auricular fibrillation.

ABSTRACT OF DISCUSSION

TESTOSTERONE IN CORONARY HEART DISEASE

QUESTION: What is the value of testosterone in coronary heart disease?

ANSWER: Testosterone is not a significant coronary vasodilator. It therefore has no significant direct effect in coronary heart disease. So far as testosterone relieves the male climacteric or removes sexual impotence, real or fancied, in the male it will alleviate the symptoms of coronary heart disease much as hormone therapy for the menopause in the female is of benefit to those women complaining of symptoms of heart disease.

VITAMIN E IN CARDIAC THERAPY

QUESTION: Has vitamin E a place in cardiac therapy?

ANSWER: Vitamin E is of no value in coronary heart disease, hypertension or rheumatic heart disease. The original claim that it is of benefit can be attributed to ceremonial therapy. The original claim has not been substantiated by any other group. We have not used vitamin E, and our opinion is therefore based on a survey of the literature and conversation with other cardiologists.

NIKETHAMIDE

QUESTION: Is nikethamide ("coramine") a cardiac stimulant or a coronary dilator?

ANSWER: There is no real evidence that nikethamide has any striking effect on the coronary vessels or on the state of the heart. Its primary action appears to be that of a respiratory stimulant and as such it has a place in certain depressions of respiratory activity which may occur in the course of heart disease.

SHOCK FOLLOWING MYOCARDIAL INFARCTION

QUESTION: How should one treat the shock that sometimes complicates acute myocardial infarction?

ANSWER: In acute coronary occlusion, i. e., recent myocardial infarction, one may find acute circulatory collapse and later

12. Weisman, S. A.: A Study of the Analeptic Value of Certain Drugs in the Treatment of Quinidine Depression, Am. Heart J. **24**: 240, 1942.

13. Scott, C. C.; Anderson, R. C., and Chen, K. K.: Comparison of the Pharmacologic Action of Quinidine and Dihydroquinidine, J. Pharmacol. & Exper. Therap. **84**: 184, 1945.

13a. Alexander, F.; Gold, H.; Katz, L.N.; Levy, R.L.; Scott, R., and White, P.D.: Relative Value of Synthetic Quinidine, Dihydroquinidine, Commercial Quinidine, and Quinine in the Control of Cardiac Arrhythmias, J. Pharmacol. & Exper. Therap. **90**: 191-201, 1947.

14. Deulofeu, V., and others: Fagarine, Possible Substitute for Quinidine, Science **102**: 69, 1945.

15. Recommendations of National Research Council Restricting the Use of Quinidine, Miscellaneous, J. A. M. A. **124**: 239 (Jan. 22) 1944: J. Pharmacol. & Exper. Therap., to be published.

this may be followed by a shock state identical to that seen during the war, or following trauma or surgical procedure. At the Michael Reese Hospital, my colleague, Dr. William Brams, in an unpublished study has indicated that desoxyephedrine appears to be successful in overcoming the vascular collapse. If his results are substantiated by further experience a worth while addition to our armamentarium is at hand. When shock develops after a recent myocardial infarction one is dealing with a real emergency, since the chance that shock will lead to death is increased in the presence of the acute damage to the heart. In shock the circulating blood volume declines and hemoconcentration occurs. It is therefore obvious that the manner of counteracting it is to add fluid to the circulation, and plasma is the ideal fluid. The risk of overloading the heart by adding plasma to the circulation is exaggerated, provided the plasma infusion is not too rapidly administered. Within limits it is not the quantity of plasma given but the rate of administration that is disturbing. The work of Altchule has shown that even the failing heart can cope with infusions into the blood stream. In the presence of a recent myocardial infarction the plasma infusion must be carefully watched in the hospital, and during its administration the level of venous pressure and the clinical state of the patient followed. Whenever the venous pressure begins to rise rapidly and in an accelerated fashion the limit of the heart is reached and the plasma should be stopped or the rate of infusion sharply decreased. It should be stopped also if rales appear in the lungs. Of course, administration of the plasma can be stopped when definite improvement of the circulation is obtained or when it is obvious that the infusion is acting detrimentally. I do not want to be misunderstood as advocating the indiscriminate use of plasma, but I believe that plasma properly administered has a definite role in cardiogenic shock with low venous pressure just as it does in traumatic and surgical shock with hemoconcentration. Of course, the risks are greater in the patient with recent myocardial infarction since the damage to the heart is the initiating cause of the shock. Nevertheless this does not negate the use of plasma, and brilliant results have been reported. Plasma in recent myocardial infarction complicated by shock is heroic therapy.

RUTIN IN HYPERTENSION

QUESTION: What is the value of rutin in hypertension?

ANSWER: The work of Griffith has been confirmed in showing that rutin tends to prevent hemorrhagic manifestations and counteracts capillary fragility. It, therefore, seems reasonable that it may be of value in counteracting hemorrhagic manifestations in hypertension. However, the final decision as to the utility of rutin must await a wider clinical experience.

HYPNOTICS AND SEDATIVES

QUESTION: What is the place of hypnotics and sedatives in cardiac therapy?

ANSWER: Hypnotics and sedatives are of value in heart disease not only by virtue of their relieving or lessening apprehension and dyspnea but also by favoring sleep. It is so common an experience that it is almost redundant to restate it, that a good night's sleep has a remarkable effect on the physical state of the patient with cardiac disease and that contrariwise a poor night's sleep has a deleterious effect. In principle, the action of hypnotics and sedatives is to decrease the twenty-four hour work and energy requirements of the body which must of necessity lessen the requirements for hard work on the part of the heart. Since the heart must completely recover during the succeeding diastole for the work it does during its systole, it is obvious that any lessening of the work requirements will be beneficial. Imperfect sleep, restlessness and emotional upsets all put added strain on the heart. They should therefore be avoided as far as possible. Dyspnea also increases the energy requirements of the body and therefore serves as a strain on the heart. Sedation which lessens dyspnea and makes breathing more deliberate therefore reduces the strain on the heart. It must also be recalled that sedatives may lessen coughing, and a cough—it must be emphasized since it is not widely enough recognized—puts a great strain on the heart. Clinicians should be concerned about these matters as much as they are about the administration of drugs like digitalis, the mercurials and quinidine.

PAPAVERINE

QUESTION: Of what value is papaverine in heart disease?

ANSWER: I still believe that papaverine has a definite place in the treatment of coronary heart disease. It is a sedative which is not habit forming. It is a "soothing agent" on ectopic pacemakers and it is one of the most powerful of the coronary vasodilators available. These statements are based on actual observation of animals and human beings. Its use intravenously should be limited to a few cases of recent myocardial infarction in which one is tempted to use morphine intravenously or in cases of recent myocardial infarction complicated by paroxysmal ventricular tachycardia. For the latter, quinidine may be used and may be more effective, but quinidine is a protoplasmic poison and when given intravenously may be hazardous. Papaverine may also be used profitably in recent pulmonary embolism. The precaution in giving papaverine intravenously is to use a slow administration over minutes, but the dose to be used should be from 1 to 1½ grains (60 to 100 mg.). There are unpleasant side effects in some instances, and there may be a profound drop in blood pressure. These are its hazards and contraindicate its use. Oral administration of papaverine may be used in recent myocardial infarction to dilate the coronary arteries, and especially when ventricular premature systoles are encountered. A large daily dosage is to be employed, 1½ grains three to four times a day. It should be stopped when any unpleasant side effects appear. Papaverine is quickly excreted and does not accumulate when given at the rate schedule suggested. It has a definite place in recent myocardial infarction, but is not universally applicable. The greatest benefit to be derived from papaverine is in chronic coronary disease complicated by angina pectoris and more especially when ventricular premature systoles are present. For the latter, however, quinidine may be preferred, although there is no reason why quinidine and papaverine may not be used simultaneously. Again, unpleasant side actions are contraindications to the use of papaverine. For chronic coronary heart disease the dose of papaverine should be begun at 1 grain three to four times a day and should be increased until the effect desired is obtained or side actions require stoppage. The aim should be to use the minimal amount per day which is effective. After a short trial, absence of any positive effect should lead to its discontinuance. Papaverine appears to have no effect on supraventricular ectopic rhythms and should therefore not be used for auricular premature systoles, supraventricular paroxysmal tachycardia, auricular fibrillation or auricular flutter. At the present time we are making a resurvey of the effectiveness of papaverine in chronic coronary insufficiency to see whether or not our early enthusiasm can be verified. We hope to be able to report on this survey within the next year.

PANEL DISCUSSION

On papers by DeGraff, Gold and Katz

PAUL D. WHITE, M.D., Boston, Moderator

DR. WHITE: It is of great importance to us all to have frequent appraisals of the value of therapeutic measures, both old and new, especially in the case of such a common and serious condition as that of disorders of cardiac function. We are fortunate to have assembled here at this centennial session of the American Medical Association several authorities on the subject. It is also a satisfaction to tell you of a most instructive exhibit on "Cardiac Drugs" prepared by one of the members of the panel, Dr. DeGraff, for the Cardiovascular Section of the Scientific Exhibit; you will find it on the main central part of the stage in the large hall of this building.

DR. GEORGE W. PICKERING, London, England: To round off this discussion perhaps I should refer to some principles in the treatment of heart disease which are not quite so new. The physician is rarely able to cure heart disease in his patients. In 9 cases out of 10 he is dealing with the management of a

chronic disease, and it is important that he should look at his patient in this light. He should for instance remember that it is easy to make an invalid out of a patient with cardiac disease by inflicting unnecessary and petty restrictions and by arousing unnecessary alarm. We learnt a good deal about the importance of psychologic factors in heart disease during the recent war, when once again the problem of neurocirculatory asthenia became acute. Many of us have suspected that the doctor might play an important part in the causation of this malady. Paul Wood provided interesting figures in support of this view. In 33 of a series of 59 recruits who had been wrongly informed that they had heart disease neurocirculatory asthenia developed, and in 26 it did not. Of the 59, 30 had a family history of cardiac neurosis or nervousness, and in 27 of these neurocirculatory asthenia developed and in only 3 it did not. In 48 subjects activity was restricted by the doctor; of these 37 obeyed and 11 disobeyed; of 28 with a positive family history 27 obeyed and 1 disobeyed the doctor's instructions. In other words, in a patient with a family history of nervous breakdowns who obeys his doctor's instructions regarding restriction of activity de Costa's syndrome is extremely likely to develop, even when the patient has no organic heart disease. Some consider, and I am one of them, that the symptoms of neurocirculatory asthenia are no less likely to develop if the patient has in fact an organic cardiac lesion. It is therefore of the first importance in dealing with heart disease that the patient should not be frightened. With regard to treatment by drugs I confess that I am a medical anachronism and that I still use the powdered leaf of digitalis in the treatment of heart failure. This became almost obligatory in Great Britain during the war because of shortage of alcohol and manufacturing difficulties. I have been satisfied with the result, and have become so familiar with the use of the powdered leaf that I have not yet seen good reason to change. I am undoubtedly conservative, but I tell myself that it is more important for a general physician who has to deal with many kinds of maladies to be really familiar with one good preparation of a potent drug than to acquire the latest refinements.

DR. GOLD: I note that Dr. DeGraff still speaks of the use of the mercurial diuretics in heart failure when patients no longer respond to digitalis. This is the traditional way of viewing the utility of the mercurial diuretics. We no longer think this correct. The mercurial diuretics represent the most important addition to the list of cardiac medications, and they are indicated in every case of congestive failure. A great deal is lost in the efficiency of treatment if we wait to put them to use only after we have discovered that the patient does not respond sufficiently to rest and digitalis. We have just completed a study in which we found that if patients with congestive failure receive digitalis and the mercurial diuretic simultaneously and systematically, immeasurably better results may be expected; namely, complete disappearance of congestive failure, in 90 instead of approximately 50 per cent of cases, and a reduction in the period of hospitalization to about one third of the time that it takes to produce complete recovery from congestive failure by the prevailing methods in which the mercurial diuretic is put to use only after digitalis has failed to bring about satisfactory results.

DR. DEGRAFF: I agree with Dr. Gold that mercurial diuretics are of utmost importance in the treatment of congestive heart failure and that the combined use of a mercurial diuretic and digitalis will relieve congestive heart failure more effectively than either one alone. However, the tendency to use mercurial diuretics alone at very short intervals in high doses not only may be dangerous but may cause the patient to suffer from severe symptoms of dehydration. Except in the later stages of their disease, most patients with heart disease can be kept free of failure by the oral use of a digitalis preparation, salt-poor diet and limitation of physical activity with occasional periods of bed rest. I do not see the necessity of giving such patients mercurial diuretics either intravenously or intramuscularly. As the heart disease progresses, a mercurial diuretic will be needed. One should at first try an oral preparation, and then if that is not sufficiently effective, the parenteral use of a mercurial diuretic is indicated. In his discussion of the cardiac glycosides, Dr. Gold has stressed the question of the completeness of absorption of digitoxin as compared with other glycosides. He failed to take into account that digitoxin has an exceedingly long latent period and a very long period of dissipation, factors which would definitely influence the experiments which he cites. As a matter of fact, whether the absorption from the gastrointestinal tract of the glycosides digitoxin, digoxin, lanatoside C and gitalin is or is not 100 per cent is not important, since extensive clinical studies by many observers have already amply demonstrated that all of these glycosides are sufficiently well and uniformly enough absorbed to be used when digitalis is indicated. In our experience, the extremely long latent period and the slow rate of dissipation of digitoxin make this glycoside less desirable for rapid oral digitalization or for maintenance than, for instance, digoxin. Should a patient become toxic from digitoxin, the symptoms may persist as long as a week, whereas toxicity is of much shorter duration with the other glycosides. Although Dr. Gold states that some patients could do with somewhat less or require more to complete the digitalization, he persists in advising a single initial dose of 1.2 mg. of digitoxin. If some patients could do with less, then why start with this dose? We find that a much safer starting dose is 0.6 to 0.8 mg., depending on the weight and age of the patient. For total digitalization with digitoxin Batterman and I have found that an average of 2.2 mg. is necessary, with the extremes of 0.8 mg. to 5.0 mg. The use of the cardiac glycosides represents an advance in treatment in that relatively pure principles are given rather than mixtures. It must be pointed out, however, that each glycoside has its own peculiarities. These are concerned not only with dosage, but with the time at which the effect begins after administration, the rate of dissipation, and the duration of toxicity.

DR. KATZ: I believe that digitalis should be given as pure glycosides in preference to whole leaf. Infusions and tinctures are going out of fashion. Our experience with digitoxin coincides with that of Dr. Gold. In addition to the slowly excreted digitoxin I would favor the use orally of some more rapidly excreted glycosides, such as digoxin and cedilanid. These latter may be used also intravenously for rapid action, but for quicker action strophanthin K or ouabain is preferable. I believe that by and large these glycosides operate in a similar fashion; their differences in action depend on the rate of their absorption and the rate of their excretion and destruction. I am sure that with time the English cardiologists will universally favor the use of pure glycosides. They are already using digoxin.

DR. WHITE: In the time that remains I shall make a few summary remarks concerning drugs in cardiac therapy. First, I want to emphasize that digitalis leaf itself in powdered form is still an effective drug in the treatment of congestive heart failure and in reducing the ventricular rate in auricular fibrillation and flutter. Its strength, of course, should be checked, but inasmuch as practically all the proprietary preparations of digitalis leaf on the market today are carefully standardized and reliable one may have much more confidence in the use of the crude digitalis leaf than was possible years ago, and, so far as I know, it still remains the least expensive way to give digitalis. As has been brought out in the discussion, the effect of digitalis is dependent on absorption, in large part at least, but there are individual variations and experience with each patient must determine the optimal dose for that patient. Certainly, as pointed out by Dr. Gold and others, digitoxin and others of the purified preparations are satisfactory now for routine use and have the advantage over the leaf itself that one may rely on the preparation quantitatively by weight without the need of standardization except on each individual patient. It would appear that we are going through a transitional period from the use of the pure digitalis leaf to the use of the pure glycosides. The transition certainly has been slow to date, however, for Nativelle as long as one hundred years ago produced the first purified glycoside (digitaline), which is our digitoxin of today. As for mercurial diuretics, one must admit that they have been a very important addition to our

therapeutic armamentarium in the treatment of congestion of all sorts, particularly that due to heart failure, during the past two decades. However, they must be suited also to the individual patient and may on occasion produce toxic effects. One of these toxic effects is due to digitalis intoxication as the result of the transfer to the circulating blood of edema and serous cavity fluids containing digitalis which may have already been given in full dosage. In the use of mercurials the intravenous route is the best and the intramuscular route second best; less satisfactory is the rectal route, and least of all oral medication. It is to be remembered that mercurial poisoning may be induced by oral therapy. Although the treatment of congestion by mercurials may be carried on for years successfully and be given even as often as every day because of the lack of accumulation, it is usually possible to reduce greatly the amount of mercurial diuretic needed or even to omit it altogether, with great benefit to the patient who may be fatigued by vigorous diuresis, if one reduces the sodium intake to a low level. During the last few years I have been able to dispense with mercurial diuretics altogether or to use them infrequently in many of my patients with myocardial failure.

I would like to add concerning the mercurial diuretics a word as to dosage. Two cubic centimeters are often too much, given either intramuscularly or intravenously, and I find that on occasion ½ cc. or even ¼ cc. intravenously has a good effect and is less exhausting. Such smaller doses may also be given more often without upsetting the patient. Ammonium chloride not only enhances mercurial diuresis but acts also by itself. It is more effective if not given constantly and it may be reserved for a few days at the time of the injection of a mercurial diuretic or it may be used three or four days at a time say every two weeks. The xanthine diuretics have been largely given up because of the greater effectiveness of mercury. As has been pointed out, morphine and Meperidine may decrease mercurial diuresis. Quinidine has come back into routine use in many places. In fact, we have never abandoned it at the Massachusetts General Hospital and I have found it helpful in many cases during the last twenty years. Its advantages far exceed its disadvantages such as its toxic effects and danger. Moreover, it should be used in prophylaxis as well as in treatment. I agree with Dr. Katz in supporting its use in coronary heart disease and have routinely given it every three to four hours in the dosage of 0.2 Gm. (3 grains) of the sulfate during the first two weeks after the onset of acute myocardial infarction. Fagarine I have not yet received from South America, although it was to have come for us to try last year. Aminophylline has its greatest value in improving respiratory function and in clearing, at least temporarily, Cheyne-Stokes breathing and cardiac asthma. It is not per se a heart stimulant. Glyceryl trinitrate I often use prophylactically in the small dosage of 1/200 of a grain (0.3 mg.) or less. Finally, I want to emphasize the value of other methods of treatment as touched on by Dr. Pickering, a proper balance between rest and activity, physical and mental, individual testing of reaction to tobacco, the importance of expert nursing, which may make the difference between success and failure, and the use of an optimistic outlook at the time of detailed explanation of their troubles to patients with cardiac disease who are usually intelligent and who, if told about their condition, are more likely to cooperate in their treatment themselves. We should constantly watch out for and seek sound new measures of treatment but also should hold on to the best measures of the past until something really better comes along. I would like to attend a panel like this after another hundred years. Perhaps there won't need to be any such panel if we can only learn about the underlying causes of heart disease and failure. In conclusion, I thank the panel members for their remarks and yourselves for your attention.

Murmurs of Congenital Heart Disease.--The murmur of patent ductus arteriosus is a continuous one lasting throughout systole and diastole, with intensification in early diastole where it covers the second heart sound and proceeds to obscure the third heart sound as well.--Evans, W.: *British Heart Journal*, October, 1947.

SARCOIDOSIS

A Review and an Appraisal

HENRY E. MICHELSON, M.D.
Minneapolis

The purpose of this paper is to assemble, to evaluate and if possible to add to the known facts about the condition for which I prefer the term sarcoidosis. The disease has been recognized for about half a century, and although many observers and investigators have contributed their findings Boeck's name will remain most prominent in the minds of students of this interesting disease. Hutchinson, Besnier, Schaumann, Darier and Pautrier have all made contributions, and in more recent years Leitner [1] and Coste [2] have helped to clarify the diverse collection of biologic and clinical findings which constitute sarcoidosis and have collected in their writings the best of the investigations and discussions anent the etiology, morphology and course of this disease.

I believe that for the present the name sarcoidosis is preferable, because it implies a wider distribution than sarcoid and emphasizes systemic involvement. Furthermore, the employment of men's names would result in a long compound title. Hunter's [3] historical sketch covers the evolution of the nomenclature. Sarcoidosis, Besnier-Boeck-Schaumann's disease, benign lymphogranulomatosis, epithelioid reticuloendothelial granuloma, noncaseating tuberculosis and other names have been proposed, but until more definite etiologic evidence supplies a term which indicates the cause of the disease, sarcoidosis would seem to be the most concisely descriptive; "sarcoid" allows complete identification, while the ending "osis" implies something more than merely a cutaneous lesion.

The present conception of this disease is that it is systemic, following a chronic course and having the characteristics of a benign infection. Its prodromal and early stages are not well known, and in most patients the lesions regress and disappear. The locations of this disease are apparently manifold; the more thorough and refined investigations became, the more tissues were added to the long list of those where sarcoid inflammation has been located.

One of the challenges that the disease presents is the difficulty and danger of a purely clinical diagnosis. No examination of a patient in whom sarcoidosis is suspected is complete without searching for lesions on the skin and mucous membranes. The superficial nodes and palpable glands as well as the eyes and small bones of the extremities should be examined, and roentgenologic studies of the thorax, hands and feet are imperative. More refined procedures such as sternal biopsy, electrocardiographic study and examination of the blood are also indicated but are not so productive of valuable evidence. Positive diagnosis rests on histologic examination, and it is doubtful whether a diagnosis of sarcoidosis can be accepted without such microscopic evidence.

The immunobiologic state of the patient is evaluated by the tuberculin test and more recently by Kveim's

From the Division of Dermatology and Syphilology, University of Minnesota, H. E. Michelson, M.D., Director.

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1. Leitner, St. J.: Der Morbus Besnier-Boeck-Schaumann, Basel, Benno Schwabe, 1942.

2. Coste, M. F.: Critères et frontières de la maladie de Schaumann, Ann. de dermat. et syph. **1-2**: 6-17 (Jan.-Feb.) 1945.

3. Hunter, F. T.: Hutchinson-Boeck's Disease (Generalized Sarcoidosis), New England J. Med. **214**: 346, 1936.

test. Because of the frequency of a negative reaction in this disease to various dilutions of tuberculin, a tremendous amount of effort has been expended in exploring the so-called positive anergy and its significance concerning a tuberculous etiology. Granting that a negative reaction cannot be overlooked, nevertheless it appears to have been overemphasized to the exclusion of a possibly more fruitful search for the presence or absence of a bacillary cause. Few investigations have been directed along bacteriologic lines other than searches for the tubercle bacillus.

Sarcoidosis may occur at any age, having been found in infants and the aged, in both sexes and in all races; however, geographic location appears to have some importance. The Scandinavian writers have certainly led in the number of articles, but the great number of patients with sarcoidosis found in the polyglot population of the United States speaks against a racial preference. In the American Negro, however, sarcoidosis, or possibly a sarcoid-like tuberculosis, is a problem by itself, and for the time being I believe that discussion and deductions would be simplified if this group of patients were kept apart until more positive knowledge is acquired. Those whose investigations are confined to Negroes have the better opportunity to establish or deny the relationship of sarcoidosis to the development of frank tuberculosis. Whether it is a transition or a complication or whether the biologic elements control the course of events should be and undoubtedly will be proved by special investigations made on this group.

EVOLUTION

The prodromal and early manifestations of sarcoidosis are not known. What may dermatologists look for as a beginning sign or symptom in such patients? It may well be that we shall continue to find the first evidences in the skin because internal lesions, even though they precede cutaneous lesions, provoke no symptoms. Some sarcoidosis patients admit that a persistent erythematous patch has existed at the site of a subsequent node, but as a rule cutaneous lesions develop insiduously. Forssman[4] critically examined some cases of erythema nodosum and erythema multiforme, with negative tuberculin reactions, having early sarcoidosis in mind. In 3 of 10 cases, using Lemming's method of injections of BCG (Bacillus of Calmette and Güerin) with subsequent histologic examination, he found pathologic reactions similar to those found in sarcoidosis. He wondered whether some cases of erythema nodosum or multiforme might not represent the acute stage of some disease, the lesions being merely a link in a chain of evidence which eventually would lead to a diagnosis. This is an attractive hypothesis and should be kept in mind when histories of patients with sarcoidosis are taken. The early cases as observed by Kyrle and Gans are well known by all students of this subject, but they bring up this query: Since the tuberculous etiology is by no means proved, are we justified in diagnosing a case as sarcoidosis, despite the histologic observations, if tubercle bacilli have been demonstrated, or are we then dealing with true tuberculosis? I would be inclined to believe the latter, and certainly so if the bacilli in addition to other unmistakable findings of tuberculosis were demonstrated.

CUTANEOUS LESIONS

It is not within the province of this paper to review again the various morphologic forms of cutaneous and subcutaneous lesions found in sarcoidosis. I do want to emphasize that almost every type of cutaneous change from erythema to formation of tumor has been attributed to this disease, by the histologic finding. I believe that we should stress the polymorphy, avoid the use of terms such as Boeck's miliary sarcoid, lupus pernio and Darier-Roussy sarcoid, and use descriptive terms such as papular cutaneous or nodular subcutaneous lesions, always retaining the diagnosis of sarcoidosis and listing the positive findings. For example: sarcoidosis with (*a*) papular cutaneous lesions; (*b*) pulmonary lesions; (*c*) enlarged inguinal nodes. One must keep in mind the decidedly atypical cutaneous lesions. I recall a patient whose lesions were indistinguishable from

Sternal preparation showing granuloma consistent with diagnosis of sarcoid.

granuloma annulare and another whose lesions looked almost like acrodermatitis chronica atrophicans. To repeat, a microscopic examination is essential, and even then only sarcoid structure can be diagnosed, not sarcoidosis.

Lesions in the mucous membrane are often described, but in my material not so often seen. The question of tonsillar biopsy offers the objection that in pulmonary tuberculosis tuberculoid infiltrate may be found in the tonsils. Involvement of the larynx and the upper respiratory tract is apparently rare in sarcoidosis as contrasted with tuberculosis.

Lymph nodes and glandular enlargements vary greatly in size and extent of involvement. In my material they are not striking, but in the reported cases the finding is frequent. The parotid, submaxillary and lachrimal glands are often reported enlarged and the syndrome of Heerfordt is of particular interest because of the rapid and at times febrile course.

Various internal glands have been invaded with symptoms provoked because of interference with a

4. Forssman, O.: Tuberculin Negative Cases of Erythema Nodosum and Erythema Multiforme, Acta med. Scandinav. **126**: 393, 1946.

5. Van Buchem, F. S. P.: On Morbid Conditions of the Liver and the Diagnosis of the Disease of Besnier-Boeck-Schaumann, Acta med. Scandinav. **124**: 168, 1946.

gland's particular function, as when the pituitary or thyroid gland has been involved.

The internal organs such as the heart, kidneys and spleen often take part in the process, but the contents of the thoracic cavity and the liver are most interesting because by means of x-ray or liver puncture one may obtain valuable evidence of the lungs and hilar glands. It need only be mentioned that here one may have lesions which are easily demonstrated and often present. Sarcoidosis involving the lungs can hardly be called a respiratory disease because as a rule it is symptomless, even though the lungs, pleura and hilar glands have extensive encroachment.

Van Buchem [5] performed liver punctures on 14 patients with sarcoidosis, results of whose hepatic function tests were normal. He found miliary sarcoid lesions in 11 of the specimens. Liver puncture offers another approach to the survey of the disease.

*Data on Patients with Proved Cases of Sarcoidosis**

Patient	Duration, Yr.	Age	Sex	Race	Skin	Nodes	Roentgenogram of Chest	Roentgenogram of Bones	Roentgenogram of Bowel	Tuberculin Reaction, 1:100	Involvement of Ear, Nose or Throat	Brucella Skin Tests
P. C.	11	54	F	W	Atrophic type	Epitrochlear	Normal	Normal	Normal	Negative	Negative	Negative
E. W.	15	41	F	W	Typical	None	Hilar	Normal	Normal	Negative	Negative	Negative
L. W.	13	50	F	W	Typical	Axillary	Normal	Toes	Normal	Positive	Negative	2 in 4 positive
O. N.	15	51	M	W	Atrophic type	Axillary	Normal	Normal	Not done	Negative	Positive	2 in 4 positive
J. M.	10	40	M	W	Plaque	Axillary (1)	Normal	Normal	Not done	Negative	Negative	Negative
A. L.	16	62	F	W	Typical	None	Interstitial fibrosis	Normal	Gastritis; narrow terminal ileum	Negative (1:500)	Negative	Not done
E. H.	8	28	F	W	None	None	Normal	Normal	Regional ileitis	Negative	Negative	Negative
G. M.	3	26	F	W	None	None	Normal	Normal	Regional ileitis	Negative	Negative	Not done
R. C.	7	34	M	W	Typical	Axillary	Hilar	Toes	Not done	Negative	Negative	Not done

Patient	Hemoglobin, Gm./100 Cc.	White Blood Cells	Monocytes, Percentage	Albumin, Gm./100 Cc.	Globulin, Gm./100 Cc.	Sedimentation Rate, Mm./Hr.	Biopsy	Comment	Response to Calciferol
P. C.	13.6	5,100	Normal	2.9	3.2	83	Tuberculoid	Cancer of uterus (treated)	Not apparent
E. W.	13.3	6,800	Normal	4.5	3.1	30	Tuberculoid	.....	Not apparent
L. W.	13	3,900	6%	4.8	1.1	38	Tuberculoid	.....	Not apparent
O. N.	15	5,800	9%	4.0	3.0	15	Tuberculoid	.....	Not apparent
J. M.	15	3,700	Normal	4.5	2.8	6	Tuberculoid	.....	Not apparent
A. L.	14	7,300	Normal	Not done	Not done	21	Tuberculoid	.....	Not apparent
E. H.	9	6,400	2-23%	Not done	Not done	81	Tuberculoid (ileum)	Skin not involved	Not given
G. M.	13	7,150	Normal	Not done	Not done	80	Tuberculoid (ileum)	Skin not involved	Not given
R. C.	14	7,300	7%	Not done	Not done	24	Tuberculoid	Cleared with no specific treatment: Mantoux reaction still negative 1:100	Not given

* There was no evidence of involvement of the eyes in any patient; general bacteriologic data indicated no abnormality; Brucella cultures were either negative or not done (patients A. L., G. M. and R. C.); Brucella agglutinations were negative or not done (patients A. L., G. M. and R. C.), and the urine of all patients was normal, as were the electrocardiograms.

ETIOLOGY

There is at present a choice of only two causes of sarcoidosis, the one being that the condition is some type of tuberculosis; the other that the disease has its own etiology. Since the theory of the tuberculous causation seems to have the most adherents, how or where is one to find the facts that finally will give irrefutable proof that the tubercle bacillus is the only cause of sarcoidosis?

Bacteriologists have searched for the cause of this disease in all of their accepted ways, and still the percentage of positive findings is much too low to be convincing. Direct methods, cultures and animal inoculations have all been tried. Special staining methods raise the percentage of positive findings a little, but on the whole attempts to incriminate the tubercle bacillus by bacteriologic means have been disappointing. Koch said that the indisputable proof of a tuberculous causation was to find the bacillus in the diseased tissue. Too few such searches have been made, and the newer methods of direct examination of excised, well identified, sarcoid lesions should be utilized.

The interpretation of histologic examination leaves much to be desired. A diagnosis of sarcoid structure can be made by this means, but the criteria on which sarcoidosis can be differentiated from tuberculosis, leprosy, brucellosis, foreign body reaction and other conditions have not been established sufficiently so that changes in the section under examination can be said to be exclusively sarcoidosis. The case reported by German [6] well illustrates this. His patient sustained an injury to the head when he fell against a canyon wall. Subsequently a tumor formed which was found microscopically to be of sarcoid structure about incorporated crystals proved to be silica. Roulet and Albertini [7] both have seen granulomas in brucellosis which were tuberculoid and could not be distinguished from sarcoid.

Neither the type of cells, the arrangement, the presence or absence of necrosis, nor the discovery of special

6. German, W. M.: Lupoid-Sarcoid Inducted by Foreign-Body (Silica), Am. J. Clin. Path. **10**: 254, 1940.

7. Roulet and Albertini, in discussion on Zollinger and Meyenberg: Ueber eigenartige perivaskulare Granulomatose des Gehirns, Schweiz. med. Wchnschr. **72**: 826, 1942.

bodies such as Schaumann [8] has found in his explorations makes it possible for a pathologist to say, "This is sarcoidosis and cannot be anything else!" When a section from a questionable case is compared with one from a positive case, it is readily seen how wide the boundary lines may be. The so-called epithelioid or naked tubercle really is not a tubercle. Certainly the large massive sarcoid structure found in true sarcoidosis is not the tuberculoid structure found in lupus vulgaris, but on the other hand areas can be found in lupus vulgaris that cannot be distinguished from sarcoidosis. Therefore the microscopic diagnosis must not be made on finding areas of massed epithelioid cells but on a survey of the entire section, and I want to repeat that the finding of an isolated so-called epithelioid tubercle, although it often is found, especially in lymph nodes, is a deceiving premise on which a diagnosis may rest. Classic sarcoidosis tissue is readily identified, but if there are observations which cast doubt on the diagnosis, it is best not to go beyond a descriptive and inclusive diagnosis. Much has been written about the age of the lesion, and still biopsies made on the same patient over a period of years have shown a surprising stability of structure. On the other hand, when a lesion is in a regressive stage, then the histology is much altered. Therefore it is not the age, but the stage of the lesion, that is important. To reiterate, before one makes a diagnosis on sarcoid structure he should demand a clinical review and weigh the evidence before making a decision.

If histology were the only basis for alining sarcoidosis with some other known condition, then one could as readily decide that it was a form of leprosy as that it was a form of tuberculosis. As a matter of fact, leprosy produces a granuloma in the skin which resembles sarcoid more than any tuberculoderma does. Leprosy offers other analogous facts too. The slow onset, the various phases and the inability to find organisms in the tuberculoid variety are points in common; there are many arguments, however, against leprosy as a causative factor in sarcoidosis.

Since there are fairly accurate tests for brucellosis, Brucella melitensis may be eliminated as the cause of this condition. There are, however, a number of similarities between the two conditions, which somewhat strengthens the view that if the bacillus of brucellosis can produce so varied a syndrome as brucellosis, then a specific organism could readily provoke all the reactions that have been found in sarcoidosis.

If dermatologists, bacteriologists and pathologists cannot definitely decide about the tuberculous etiology of sarcoidosis, where may one expect to find help? I believe that it should come from the experts in tuberculosis. Can this array of findings which make up sarcoidosis be accepted as a type of tuberculosis? Does any known form of undisputed tuberculosis offer comparable findings? Mylius and Schürmann,[9] Pinner,[10] Hagn-Meincke [11] and others have compared sarcoidosis with noncaseating tuberculosis or with indolent tuberculosis, but patients with this condition have pulmonary tuberculosis which may and often does change in type and become one of the more serious forms of the disease. Furthermore, in patients with this chronic productive type of tuberculosis, even though there may occasionally be concomitant lesions, such as ocular or osseous lesions, they are not found with nearly the regularity that they are in patients with sarcoidosis; also the prognosis in patients with indolent tuberculosis rests largely on the course of events in the patient's life. Undue stress and strain, a concurrent infection or residence in an unfavorable climate may and often does bring about dire consequences, but patients with sarcoidosis do not seem to be so affected. If sarcoidosis is a form of tuberculosis, then the indolent form of tuberculosis so well described by Gloyne [12] best affords comparison; yet sarcoidosis is very different. Tuberculosis rarely if ever yields such extensive findings as does sarcoidosis. The tubercle bacillus seems to select its tissue and confine its ravages there. Patients with lupus vulgaris rarely have active glandular, osseous and pulmonary tuberculosis in addition to cutaneous lesions. Having a close association with Glen Lake Tuberculosis Sanatorium for a long period impressed me with the fact that patients with mixed tuberculosis are rare. The number of cases of pulmonary tuberculosis in which lesions of skin, bone or gland developed was comparatively small. A review of patients with sarcoidosis, on the other hand, reveals that almost all of them had disseminated lesions and that involvement of only one organ system was the exception. In this respect the two conditions are entirely different. Tuberculosis ignored progresses. An organized regimen, active treatment, awareness of the possibilities and cooperation are necessary to cure or check the disease. Sarcoidosis may be entirely ignored, and with few exceptions the patient does just as well, or better, than with medical intervention. There is an environmental and family factor in tuberculosis. Great stress is laid on finding the infecting source—the contact. Patients with sarcoidosis share their condition with no one in their immediate sphere. There are few contact cases. If the tubercle bacillus is the cause, can the patient with sarcoidosis render the bacillus noninfectious to others? It is hard for me to accept the tuberculosis theory of etiology.

The epidemiology and pathogenesis of tuberculosis have been the subject of a vast amount of research, and regardless of one's particular views certain well known facts have become established. For example, the changing clinical types, the effect of the times—the increase in tuberculosis in war-torn countries and the influence of organized control—but sarcoidosis goes serenely on in its own peculiar way.

Thanks to the work of Ghon and his pupils, the primary focus is accepted as the starting point of tuberculosis. Do patients with sarcoidosis have a primary lesion? If so, is it in the lung and if in the lung does it have the histology of sarcoid? Obviously these are difficult questions to answer. A number of years ago I wrote to Professor Ghon and asked whether they had ever encountered a primary focus which showed sarcoid structure. Dr. Rudolf Bezecny answered that they had not. This may not mean much, but if the patient with sarcoidosis has such unusual resistance to tubercle bacilli, is he born that way or does he acquire this reactional partial immunity? The power to sup-

8. Schaumann, J.: On the Nature of Certain Peculiar Corpuscles Present in the Tissue of Lymphogranulomatosis Benigna, Acta med. Scandinav. **106**: 239, 1941.

9. Mylius, K., and Schürmann, P.: Universelle sklerosierende tuberkulöse grosszellige Hyperplasie, eine besondere Form atypischer Tuberkulose, Beitr. z. Klin. d. Tuberk. **73**: 166, 1929.

10. Pinner, M.: Noncaseating Tuberculosis, Am. Rev. Tuberc. **37**: 690, 1938.

11. Hagn-Meincke, F.: Boeck's Sarcoid and Its Relation to Tuberculosis, Acta tuberc. Scandinav. **18**: 1, 1944.

12. Gloyne, R.: Indolent Tuberculosis, Tubercle **27**: 106, 1946.

press the tuberculin reaction must either be inherent or acquired if the cause of sarcoidosis is tuberculous. Surely the microbe does not explain this, for in cases in which the bacilli were found they have not been the attenuated types.

No amount of conjecture will solve this problem. It must be approached with well directed research.

Dermatologists, and I believe oculists, have been all too willing to diagnose a variety of conditions on a purely morphologic and histologic basis as being tuberculosis. I need only to mention with what alacrity dermatologists diagnose rosacea-like (micropapular) tuberculid with no confirmatory evidence of tuberculosis.

Since pathologic reactions have been provoked by various agents which result in microscopic findings that are indistinguishable from sarcoid, the view that sarcoidosis is not a specific disease, but rather a type of response, has been accepted by certain observers. That histologic evidence characteristic of sarcoid may be found in many conditions is true, but patients who have the disease called sarcoidosis have other confirmatory manifestations, and all such patients have so much in common that to me it appears that there must be a common etiologic agent.

Tuberculosis, leprosy and brucellosis occur in various forms, and still there is always enough evidence so that the disease is diagnosed as such. Syphilis also is protean in its manifestations, but for this disease there are specific remedies and one sees this great variety of lesions respond to a single drug with equal rapidity. Another proof of its entity.

The Kviem test if perfected will be of great diagnostic value. It should be of immense value in investigating sarcoidosis. Especially should it help in excluding tuberculosis, if that is possible, but researches should be directed toward discovering an etiologic agent.

In order to procure a base line co-workers and I decided to hospitalize patients with proved cases of sarcoidosis and study them with all the means at our command.

What do we learn, then, from these findings? 1. The history throws no light on the onset or prodromal signs of this disease. 2. The patients all were in reasonably good health, although in 1 case (Mrs. W.) there were periods of ill health and these periods were associated with the appearance of new lesions in previously uninvolved areas. 3. Roentgenologic examination of the thorax, feet and hands yielded evidence of the disease in some cases and in these instances was of definite value in diagnosis. 4. The histology of cutaneous lesions was diagnostic and hence the more characteristic the lesions were, the more indubitable was the microscopic diagnosis. 5. Examination of material obtained by sternal puncture was valuable and in 1 instance showed evidence of granuloma that was consistent with the other findings but alone would not have permitted making an unequivocable diagnosis of sarcoidosis. 6. Extensive studies (Drs. Wesley Spink, Wendall Hall, A. I. Braude) failed to reveal any connection between sarcoidosis and brucellosis in 8 classic cases of sarcoidosis.

CONCLUSIONS

1. Sarcoidosis is the best term at present to designate this condition. Sarcoidosis usually involves a number of different tissues and the patient should always be examined for extensive distribution. The disease is usually benign in its course and more or less self limited. No treatment known to date brings about rapid disappearance of the lesions. Vitamin D_2 therapy, although worthy of more extensive trial, has not been nearly as effective as in lupus vulgaris. The cause is not yet known and the explanation for the anergy often present in this condition is not clear. Microscopic study of excised lesions permits a diagnosis of sarcoid structure, but the diagnosis of sarcoidosis must be based on the sum total of the evidence obtained in each case.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: As usual, Dr. Michelson's presentation has been most lucid. His paper is comprehensive and closely reasoned. On the perennial question of nomenclature, I would accept the substitute of "sarcoidosis," provided it were established that every case of what we are pleased to call sarcoid was a widely disseminated disease. I wonder if that is quite the case. I feel sure that the majority of cases of Boeck's sarcoid (what we call that) do not present demonstrable evidence of widespread dissemination. Time and time again in our society presentations, the report is that the bones were examined roentgenologically; the mediastinum did not show any hilar enlargement; the lymph nodes were not eglarged. In other words, it appears that the disease was not widely disseminated. I would prefer until that time has arrived to stick to sarcoid. After all, dermatologists have priority in the matter. Dermatologists used sarcoid before the internists used sarcoidosis. Of course, when the cause is discovered we may think differently. The second point is the matter of the analogous diseases which Dr. Michelson had to exclude. He mentioned brucellosis, and that is one of the highest points in his presentation. He has excluded that as the explanation of the sarcoid reaction. I would like to add one more, namely, leishmaniasis. I have seen a sarcoid type of reaction in leishmaniasis. As to the American Negro, I agree with him entirely. Dr. Klauder and I were careful when we reported a very early case of this disease to give it a different title from sarcoid. We called it "Multiple Sarcoid-like Granulomas of the Skin of Undetermined Nature" (Arch. Dermat. & Syph. 13: 374-379 [May] 1926). Finally, the histology: What Dr. Michelson said about sarcoid holds good for a host of other dermatologic conditions. There are many expressions of change of other diseases in which a given picture in a given subject will not be diagnostic. That goes for syphilis, tuberculosis, many inflammatory and other dermatoses. In syphilis it is only occasionally that there are enough criteria whereby we can state that the dominant character favors a diagnosis of syphilis.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: Ray and Shipman in 1923 showed that epithelioid cell tubercles could be produced with chloroform-soluble lipins of the tubercle bacilli. Defatted and chloroform-soluble lipins from grass and colon bacilli produced the same type of lesions; the former associated with many giant cells. Florence Sabin, while observing the cellular changes in the milk spots of the omentum of rabbits, saw monocytes and clasmatocytes pick up injected phosphatide and become transformed into epithelioid cells and Langhans giant cells. Her studies also showed that animals, given antigenic amounts of the phosphatide, would develop antibodies to it. With Smithburn, she later showed that when the typical cellular response to the phosphatide was produced—and she thinks the epithelioid cell reaction can be called the phosphatide phase of the disease—hypersensitiveness to tuberculin did not occur. This may have some bearing in the positive anergy reaction so often seen in sarcoidosis. W. M. German reported a case of sarcoid-like lesion appearing in an old scar fourteen years later, in a mountain climber who fell and injured his scalp. He excised the tumor. Pathologic examination of the lesion showed whorls and masses of epithelioid cells and giant cells of the foreign body type. In the latter, particles of silica were seen, and he postulated that silica was the causative fac-

tor. He suggested that perhaps silicosis could produce a foreign body reaction similar to sarcoid. The late Dr. Gardner at Saranac Lake continued this work and showed that the injection intravenously of silica dioxide produced lesions in liver, bone and lymph nodes indistinguishable from tuberculosis. When it was inhaled, similar lesions occurred in the lungs. J. T. Fallon, in Canada, who continued the work of Gardner, found exactly the same thing that has been described by Gardner and was impressed by the amount of phospholipid associated with lesions in the lungs produced by silica dioxide which had been inhaled by rabbits. The silica-free phosphatide was extracted from the lungs and then introduced into the lungs of fresh animals. The same epithelioid cell response occurred. From this work one might infer that the naked tubercule of epithelioid cells characteristic of sarcoid may have several etiologies, but that behind its production lies a fat compound of the phosphatide type. In the work reported by Drs. Grekin and Taylor and myself in the *Journal of Investigative Dermatology*, Sept. 1947, on the treatment of sarcoidosis with calciferol and dihydrotachysterol (Curtis, A. C.; Taylor, H. and Grekin, R. H.: Sarcoidosis: I. Results of Treatment with Varying amounts of Calciferol and Dihydrotachysterol, J. Invest. Dermat. 9:131, 1947) it is our belief that these agents operate, not through their effect on calcium, but because they have some effect on the phosphorus of the phosphatide, which we think is important in the development of sarcoid lesions.

DR. HENRY E. MICHELSON, Minneapolis: I think if Dr. Weidman wishes to retain the term "sarcoid" that it should apply only to a local lesion, but if one looks long enough and far enough, one is apt to find other lesions, and therefore I prefer the term "sarcoidosis." As to the experimental work that Dr. Curtis mentioned, one must remember that in such experiments one produces lesions, not the disease. Sarcoidosis as a widely spread disease is one thing and a local lesion produced experimentally is another. German's case, in which silicate was the irritant, was interesting but it only emphasized what Dr. Oppenheim and others have brought out before, that local irritants, insoluble and unabsorbable, may produce this type of reaction. In a recent issue of *Acta dermato-venereologica* a fungoid cause for sarcoidosis was proposed, and it is worthy of consideration. About vitamin D_2, one must remember that almost all good drugs may be poisons when used in high enough dosage. Since sarcoidosis is a comparatively benign disease, I would be loath to use toxic doses of vitamin D_2 in an effort to make lesions disappear.

Innervation of the Carotid Sinus.—There are four nerves which contribute to the innervation of the sinus and adjacent carotid body, namely, the glossopharyngeal, vagus, cervical, sympathetic, and hypoglossal. The branch to the hypoglossal is inconstant and the part played by this nerve is probably not important. The other three nerves show considerable variation to their gross anatomic arrangements but great constancy in their connections to the carotid sinus and the intercarotid plexus. Embryologically the mesoderm of the third branchial arch artery and the ectoderm of the glossopharyngeal nerve possess an early juxtaposition in the region which is the anlage of the carotid body and carotid sinus; elements from the sympathetic and the vagus enter only at a comparatively late stage of development. From anatomic dissection it has been shown that a distinct and constant branch of the glossopharyngeal nerve connects with the sinus and intercarotid plexus. The importance of this nerve is supported by its striking constancy in all species of animal. Ray, S., and Stewart, J.: *(Surgery,)* March 1948.

Clinical Notes, Suggestions and New Instruments

RELIEF OF MORPHINE ADDICTION BY PREFRONTAL LOBOTOMY

T. H. MASON, M.D. and W. B. HAMBY, M.D.

Buffalo

Since the development of psychosurgery, initiated by Egas Moniz [1] in 1935 and later advanced by Freeman and Watts [2] in the United States, therapeutic results have been attained in mainly two fields of endeavor; one in psychiatry, the other directed toward the relief of intractable pain. This case report analyzes a heretofore unrecorded situation of an unusual type of chronic pain associated with the habitual use of tremendous quantities of morphine sulfate, being relieved by prefrontal lobotomy.

REPORT OF CASE

Mr. A. C., a draftsman aged 39 years, was admitted to the Buffalo General Hospital on June 16, 1947. Three years earlier he had sustained a laminectomy for spinal epidural abscess extending from the eighth to the twelfth dorsal vertebra. He survived with spastic paraplegia, a sensory level reaching approximately the nipple line and sphincter difficulty. Over the intervening three years he had been nursed efficiently by his wife. About six months after discharge from the Buffalo General Hospital he first began to complain of excruciating pain which he described as an unbearable "curling of the toes." Later there developed sensations such as "squeezing of the testicles, clawing of the perineum," and intense "burning in the rectum." These were controlled by hypodermic injections of morphine sulfate. Increment from time to time was necessary to alleviate his pain. Equally harassing was his fear of failure to receive medication, so that about half of each interval was spent in reminding his wife not to forget the injection. Finally he was receiving 42 grains (2.73 Gm.) of morphine sulfate daily.

Examination revealed a pleasant, young-appearing, 42 year old man who seemed comfortable and well adjusted to his situation. Patchy leukoderma was seen over the right lower jaw. There was full range of motion of the upper extremities, and motor power was good. Total areflexia was present below the eighth dorsal vertebra with flaccid paraplegia and bilateral foot drop. Anesthesia extended downward from the nipple line, above which was a 3 inch (7.6 cm.) band of hyperesthesia. The anal sphincter was atonic, and catheterization was required to empty the bladder.

He was made comfortable by the accustomed dose of morphine, 7 grains (0.45 Gm.) every four hours. Without this he complained bitterly of pain and became irritable and restless. No earnest attempt was made to withhold the opiate because of the fear of severe withdrawal symptoms. The bladder was controlled by tidal drainage and small trophic ulcers were given special attention. Because of the good results from prefrontal lobotomy for relief of intractable pain obtained by Poppen [3] and ourselves, this procedure seemed desirable here.

On the third hospital day a prefrontal lobotomy was performed through bilateral coronal parasagittal trephine openings. During the immediate postoperative period the patient twice was given morphine sulfate, 1½ grains (0.09 Gm.) and later two individual doses of ½ grain (0.03 Gm.) each, for restlessness. After thirty postoperative hours had passed, the patient seemed to be doing well, and morphine was withdrawn completely. He showed the usual immediate effects of lobotomy, such as apathy, unconcern, disorientation, tactlessness and loss of initiative. His appetite increased. The complaint of pain in the head was expressed occasionally, but this was fleeting and

From the Buffalo General Hospital and University of Buffalo School of Medicine.

1. Moniz, E.: Les premieres tentatives operatoires dans le traitement de certaines psychoses, Encephale 31:1, 1936.
2. Freeman, W., and Watts, J. W.: Prefrontal Lobotomy in Agitated Depression: Report of a Case, M. Ann. District of Columbia 5:326, 1936.
3. Poppen, J. L.: Prefrontal Lobotomy for Intractable Pain, Lahey Clin Bull. 4:205, 1946.

did not seem to disturb him. Injections of morphine were forgotten. He toyed and fussed with whatever was within reach. He became progressively more rational and conversational. Memory was good though emotional affect was lost. The patient remained moderately overactive and was discharged on the eleventh postoperative day in good condition.

Five months have passed since the operation, and he requires no opiates. He is rather comfortable and about to begin a course of paraplegic rehabilitation, toward which he was refractory prior to operation.

COMMENT

Dual effects were attained in this case of cord stump pain associated with severe narcotic addiction. The unbearable sensations which had been referred to anesthetic zones no longer disturbed him. His crying need for opiate and hypodermic relief was forgotten; all anxiety, emotion, foresight and insight in relation to pain were lost. Amnesia for the surgical treatment was present, but this has been a frequent result of disruption of frontal association and projection pathways. A small amount of morphine was given immediately after the operation because of apprehension in regard to withdrawal symptoms. As the patient began to show a good recovery on the second postoperative day, it was decided to withhold morphine completely, undesirable effects being watched for.[4] Severe withdrawal symptoms such as diarrhea, loss of weight and persistent vomiting did not occur, nor did the more moderate abstinence effects, dilated pupils, anorexia and gooseflesh. On the first and third postoperative days intermittent tremors were present in the left shoulder and hand. These were brief and sporadic, and may have been associated with the removal of morphine. Restlessness and overactivity that were present have been seen both in the abstinence syndrome and after lobotomy, so they could not be dissociated. It is common for addicts from whom narcotics have been withheld to manifest daily fever, increased respiratory rate, insomnia, yawning, lacrimation and diaphoresis.[4] These were not experienced by the patient.

There has been considerable discussion as to whether the so-called withdrawal symptoms are organic or psychic in origin. Light and his co-workers[5] in 1929 seemed convinced that there was an organic basis for the syndrome so commonly found. Goodman and Gilman[6] stated that symptoms start within four to twelve hours after the last dose of morphine is omitted and reach their peak in ninety-six, and then decline. This period coincides with our patient's slight tremors in the left upper extremity and restlessness.

This evidence would suggest that withdrawal symptoms are largely within the psychic sphere. Lobotomy, which nullifies emotional tension, in this case removed the psychologic necessity for morphine, leaving only the organic component for analysis. The only objective organic effect was mild tremor.

Davis and Martin[7] have described recently a type of diffuse burning pain in spinal lesions which is not relieved by cordotomy. It is thought to be transmitted over autonomic pathways to enter the cord at various levels. Our patient's pain seems to fall within this category. It is now fairly well accepted that intractable pain may be relieved by severing the frontal association and projection pathways.[3] This has been done with good results in cases in which the patient had been accustomed to therapeutic doses of opiates for the relief of chronic, unbearable pain. By personal correspondence[8] and review of the medical literature, we have found no previous record of the cure of morphine addiction by prefrontal lobotomy. It is not implied that psychosurgery should be resorted to in uncomplicated cases of opiate addiction. When addiction is associated with possible organic cause for pain and cannot be broken by medical or psychiatric therapy, lobotomy may prove useful. The results here suggest that withdrawal symptoms are for the most part within the psychic sphere, although no general conclusions can be reached from a single case study.

SUMMARY

An unusual type of persistent pain and an associated severe morphine addiction in a paraplegic patient were relieved by prefrontal lobotomy. Prompt removal of the drug on the second postoperative day produced relatively no withdrawal symptoms. It is suggested that the latter group of symptoms are largely psychic.

ADDENDUM

Since this article was submitted for publication it has come to our attention that a case reported by J. L. Poppen in the *Lahey Clinic Bulletin* (4:205, 1946) had relief of morphine addiction and intractable facial pain.

4. Himmelsbach, C. K.; Eddy, N. B., and others: Clinical Studies of Drug Addiction, Pub. Health Rep., 1938, supp. 138, pp. 114-129.
5. Light, A. B., and Torrance, E. G.: Opium Addiction, Arch. Int. Med. 44:376 (Feb.) 1929.
6. Goodman, L., and Gilman, A.: Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, p. 214.
7. Davis, J., and Martin, J.: Studies upon Spinal Cord Injuries, J. Neurosurg. 4:6, 1947.
8. Freeman, W.: Personal communication to the authors.

Council on Physical Medicine

REPORT OF THE COUNCIL

The Council on Physical Medicine has authorized publication of the following article:

HOWARD A. CARTER, *Secretary.*

EXPERIMENTAL PRODUCTION OF CANCER OF THE SKIN BY ULTRAVIOLET RADIATION

Its Implications in the Use of Sunlamps

W. W. COBLENTZ, Ph.D.
Washington, D. C.

Some fifteen years ago when the Council on Physical Medicine first undertook the formulation of specifications for accepting so-called sunlamps, qualitative experimental data were available to indicate the possibility of producing cancer on the ears of mice by excessive, often repeated doses of ultraviolet radiation. It was also known qualitatively that relatively small doses of ultraviolet radiation of wavelengths shorter than 2,800 angstrom units produce keratitis and conjunctivitis.

The sunlamps which were then on the market ranged from nondescript products to hot quartz mercury arc lamps which are suitable only for professional use. Hence, after consultation with recognized authorities regarding the potential hazard of initiating cancer of the skin and the unquestionable hazard of causing conjunctivitis, and also with the Food and Drug Administration on what constitutes misbranding, standards for the acceptance of sunlamps[1] were promulgated.

In recent times quantitative data have been published on the spectral quality and total intensity of ultraviolet radiation required to produce erythema, keratitis, cancer of the skin and the like. The energy relations involved in these physiologic reactions form an interesting study, the results of which I now summarize.

Erythema.—A minimum perceptible erythema is defined as a reddening of the skin that disappears in fifteen to twenty hours after irradiation.

The erythema test now in common use is a quick, safe method of determining skin tolerance, which is especially important before irradiating large areas of a (blond) nontanning skin.

The spectral range of ultraviolet wavelengths in sunlight that produce erythema extends from about 2,900 to about 3,200 angstroms. To qualify as a sunlamp an artificial source must emit a specified minimum amount of ultraviolet radiation in this wave band.[1] This correlation was worked out about fifteen years

1. Acceptance of Sunlamps, J. A. M. A. 102:42 (Jan. 6) 1934; 114:325 (Jan. 27) 1940; 118:298 (Jan. 24) 1942; revised, 1947.

ago by irradiating untanned persons with skin of average pigmentation.[2]

To produce a minimum perceptible erythema on exposure to midsummer, noon hour sunlight, at sea level, requires from 1 to 2 million ergs/sq. cm.,[3] depending on the dryness of the skin.

The ultraviolet energy required to produce a minimum perceptible erythema, using sunlamps of types S 1 and R S, averages about 1,100,000 ergs/sq. cm.

In my tests of several makes of type R S sunlamps an exposure of three times the minimum perceptible erythema dose did not produce burns, but it left a tan that remained for one to two months.

As described elsewhere,[4] in sunlamps of types S 1 and R S the biologically effective radiation is emitted mostly in the intense emission lines of the high vapor pressure mercury arc, of wavelengths 2,967, 3,024 and 3,134 angstroms; and while the spectral energy distribution throughout the whole spectrum (ultraviolet, visible, infrared) is not closely similar to that of solar radiation, the same biologic effects are obtained. This is because the discrete emission lines happen to occur in the proper wavelengths and intensities to produce the same biologic effect as the more continuous but less intense spectrum of ultraviolet radiation that is integrated over the wave band extending from about 2,900 to 3,200 angstroms in sunlight at sea level.

Cancer of the Skin.—In determining the band of wavelengths specific in producing cell changes that lead to cancer on the ears of white mice Rusch, Kline and Baumann[5] used low vapor pressure cold quartz lamps (radiation of wavelength 2,537 angstroms) and high vapor pressure hot quartz mercury arc lamps, in which the filtered, "midultraviolet" radiation consisted principally of wavelengths 2,967, 3,024 and 3,132 angstroms, that occur in spectral quality but not necessarily in relative spectral intensity in types S 1 and R S sunlamps.

Data are given on the results of a daily carcinogenic dose of 35.7 million ergs/sq. cm. of "ultraviolet energy" (wavelengths 2,000 to 4,000 angstroms). This was equivalent to 6 to 8 million ergs/sq. cm. of "midultraviolet" radiation, or six to eight times the minimum perceptible erythema dose tolerated on the human skin, and equivalent to a second or third degree erythema when exposed to a type S 1 or R S sunlamp. Certainly such a dose could not be repeated day after day on the human skin.

They reported that, using carcinogenic amounts of radiant energy, well defined erythema occurred early in the experiments but subsided somewhat after three or four weeks. In some instances the ears of the white mice became ragged or stubby, but that did not seem to affect the incidence of cancer.

After continuing the exposures for one hundred and thirty-five days 44 per cent of the mice in group I (24 mice in a group) and 55 per cent of those in group II had tumors.

The results pertinent to the present discussion are that the "midultraviolet" energy (essentially of wavelengths 2,967, 3,024 and 3,132 angstroms) necessary to produce carcinogenesis in 50 per cent of the group of mice ranged from 672 to 2,360 million ergs/sq. cm. over the irradiation period of one hundred and thirty-five days, with a mean value of 1,598 million ergs/sq. cm. The incidence of tumors ultimately reached 70 per cent after one hundred and seventy days of irradiation.

The daily exposures to cold quartz mercury arc radiation (principally of wavelength 2,537 angstroms) for a much longer period and a much larger total dosage (5,712 million ergs/sq. cm.) produced no tumors. In contrast, as will be noted presently, a momentary exposure to only a small fraction of this amount of radiation from a cold quartz lamp is sufficient to cause conjunctivitis and keratitis.

By using these enormous doses of ultraviolet radiation, frequently applied, it was possible to show which particular band of wavelengths is specific in initiating cell changes that lead to cancer. In this respect it is an extremely important contribution to science.

The concomitant physiologic and photochemical reactions that are produced on much smaller doses of ultraviolet radiation of these same wavelengths will now be summarized.

Ultraviolet Radiation Therapy in Human Rickets.—An important use of a sunlamp is in a children's playroom, for the prevention of rickets. When the type S 1 sunlamp was first introduced, Gerstenberger and Russell[6] studied its efficiency as an antirachitic factor. For this purpose 2 (3 at the start) rachitic patients were exposed once a week, front and back, to a type S 1 sunlamp for a sufficient time to produce a definite erythema. Two of the infants were Negro and 1 was Italian. In other words, the skin was pigmented and presumably tolerated a greater dosage than could be given to a blond skin.

None of these patients showed progressive healing at the beginning of the treatment by ultraviolet radiation. Two weeks after treatment was begun (after two irradiations) the roentgenograms showed the beginning of healing, which was complete in five weeks in the infant with moderate rickets and in seven weeks in the (white) infant having severe rickets.

In other words, of the 2 patients for whom complete records were obtained, 1 had received five and the other seven irradiations that produced a definite erythema, which, according to the description of the authors, was an exposure of about two and one-half times as long as that required to produce a minimum perceptible erythema now commonly used as a maximum exposure.

From this I deduce that the single dose was about 2 to 2.5 million ergs/sq. cm., or a total of 10 to 12.5 million ergs/sq. cm. in the five treatments of the infant having moderate rickets and a total of 14 to 17.5 million ergs/sq. cm. during the seven irradiations of the infant having severe rickets.

In contrast, as previously described, using filtered radiation from a hot quartz mercury arc lamp, of wavelengths 2.894, 2,967, 3,024 and 3,132 angstroms, the total ultraviolet energy used in producing tumors on the ears of 50 per cent of a group of white mice was

2. Coblentz, W. W.; Stair, R., and Hogue, J. M.: Tests of a Balanced Thermocouple and Filter Radiometer as a Standard Ultraviolet Dosage-Intensity Meter, Bur. of Stand., J. Research **8**: 759 (June) 1932.

3. This is an abbreviation for the cumbersome "erg seconds per square centimeter."

4. Coblentz, W. W.: Sources of Ultraviolet and Infrared Radiation Used in Therapy, J.A.M.A. **132**: 378-387 (Oct. 19) 1946.

5. Rusch, H. P.; Kline, B. E., and Baumann, C. A.: Carcinogenesis by Ultraviolet Rays with Reference to Wavelength and Energy, Arch. Path. **31**: 135-146 (Feb.) 1941. See their paper for bibliography of earlier work.

6. Gerstenberger, H. J., and Russell, G. R.: Sunlight Type S-1 Lamp (G. E.) Therapy in Human Rickets and Rachitic Spasmophilia, J. A. M. A. **94**: 1049-1050 (April 5) 1930.

roughly one hundred and fifty to two hundred times the energy used in curing rickets in children with ultraviolet radiation from a type S 1 sunlamp emitting the same wavelengths and having, presumably, closely the same relative spectral intensities as used in the carcinogenic experiments.

Subsequent investigations by Gerstenberger and Horesh [7] and by Knudson [8] show that such heavy doses of ultraviolet radiation are not necessary, especially to prevent rickets. Moreover, infrequent irradiation seems to permit regeneration of injured tissue, if any injury occurs.

Pathologic Effects of Ultraviolet Radiation on the Eye.—In their investigations of the effect of ultraviolet on the eye Verhoeff and Bell [9] used heterogeneous radiation from a hot quartz and a magnetite arc lamp. Exposures were made on the eyes of rabbits and monkeys and on one human eye.

They found that the liminal exposure capable of producing photophthalmia to the extent of conjunctivitis accompanied by stippling of the cornea, in terms of ultraviolet radiation of wavelengths shorter than about 3,050 angstroms (determined by a filter method), was approximately 2 million ergs/sq. cm. If a factor is applied to include the recently determined [10] spectral keratitic response to an equal energy stimulus, their value is reduced to less than 1 million ergs/sq. cm.

In recent times, in connection with an investigation of injury to the eye from ultraviolet radiation in arc welding (using 300 to 400 amperes) Kinsey, Cogan and Drinker [11] found that the energy necessary to produce keratitis in man by ultraviolet radiation is approximately two thirds that required in rabbits.

On exposure of human beings at a distance of 7 feet (213.36 cm.) from a 300 ampere arc they found that ocular lesions were produced in thirty seconds. From their intensity measurements, made with a tantalum photocell calibrated against a cold quartz mercury arc lamp, I deduce that the ultraviolet energy (heterogeneous iron arc radiation of wavelengths shorter than 3,000 angstroms) required to produce keratitis was about 45,000 ergs/sq. cm. of equivalent 2,537 angstrom radiation. This value seems extremely low. It is important to note, however, that the uncomfortable gritty sensation caused by stippling of the cornea and by conjunctivitis is felt after much shorter exposures and lower intensities than those used in the herein described experiments on the eyes of animals. This I know from numerous personal experiences extending over a period of more than three decades, when ultraviolet radiation from a hot quartz mercury arc lamp was sometimes accidentally flashed back of my spectacles, causing a mild conjunctivitis on the outer corner of the eye.

An important paper by Cogan and Kinsey [10] gives the spectral keratitic reaction which requires the least energy (150,000 ergs/sq. cm.) using homogeneous radiation of wavelength 2,880 angstroms, in comparison with 180,000 ergs/sq. cm. to produce a minimum perceptible erythema with a wavelength of 2,967 angstroms.[12]

Using homogeneous radiation of wavelength 2,520 angstroms, 600,000 ergs/sq. cm. was required to produce a threshold keratitic reaction, in comparison with about 365,000 ergs/sq. cm., in summer and 750,000 ergs/sq. cm. in winter [12] to produce a minimum perceptible erythema with radiation from a cold quartz lamp emitting the same wavelength, 2,537 angstroms.

In practice the erythema produced by this amount of radiation of wavelength 2,537 angstroms is so evanescent (observable for only a short time, some three hours after irradiation) that easily twice that amount of radiation is applied to get a definite (minimum perceptible erythema; one that lasts ten to fifteen hours) reddening of the skin of average pigmentation, with no ill effects. On the other hand, photophthalmia is a painful experience with no factor of safety from injury, on overexposure.

These data show that practically the same amount of energy of wavelength 2,537 angstroms causes photophthalmia as is required to produce a minimum perceptible erythema on untanned skin. Hence, in irradiating the body with the cold quartz mercury arc lamp, unless eye-protective glasses are worn there is no factor of safety between a dose giving minimum perceptible erythema and photophthalmia consisting of conjunctivitis accompanied by stippling of the cornea.

Other objectionable features (such as deactivation of ergosterol) in using ultraviolet radiation of wavelengths shorter than about 2,800 angstroms in the home without the supervision of an experienced technician are summarized elsewhere.[13]

In a recent paper entitled "Ultraviolet Action Spectra," presented at the Chicago meeting (May 18 to 22, 1947) of the Federated Societies of Experimental Biology, Bachem [13] criticizes the Council on Physical Medicine for accepting sunlamps for home use without medical supervision, his objection being that they contain a "spectral range which permits easy burning and blistering and may produce skin cancer."

In his opinion "the proper spectrum for home lamps should contain the 2,600 and 3,600 angstrom areas without the 3,000 angstrom range." He does not consider the hazard of causing keratitis and conjunctivitis by radiation of wavelengths shorter than 2,800 angstroms a problem that (beginning with Louis Bell [9]) has claimed my attention for more than three decades in connection with the protection of industrial workers in electric welding and the like.

The only practical source that is available to emit the short ultraviolet wavelengths suggested by Bachem [13] is the low vapor pressure cold quartz mercury arc lamp with a strong emission line at 2,537 angstroms, which, as is well known, constitutes about 98 per cent of the total biologically effective radiation of 3,132 angstroms and shorter wavelength.[14]

To use ultraviolet radiation of these short wavelengths in so-called "home lamps" because they do not initiate cell changes that may perhaps produce cancer is impracticable because of the danger of causing photophthalmia. This is a certainty as just noted, unless glasses are worn, which is not enforceable in the home. On the other hand, from the foregoing analysis of the data on the

7. Gerstenberger, H. J., and Horesh, A. H.: The Cure of Infantile Rickets with Tungsten Filament Radiation, J. A. M. A. **97**: 766-770 (Sept. 12) 1931.

8. Knudson, A.: Rickets: Comparative Value of Several Light Sources for the Cure and Prevention, Am. J. Dis. Child. **44**: 531-541 (Sept.) 1932.

9. Verhoeff, F. H., and Bell, L.: The Pathological Effects of Radiant Energy on the Eye, Proc. Am. Acad. Arts & Sc. **51**: 630-793 (July) 1916. Includes a very complete bibliography.

10. Cogan, D. G., and Kinsey, V. E.: Action Spectrum of Keratitis Produced by Ultraviolet Radiation, Arch. Ophth. **35**: 670-677 (June) 1946.

11. Kinsey, V. E.; Cogan, D. G., and Drinker, P.: Measuring Eye Flash from Arc Welding, J. A. M. A. **123**: 403-404 (Oct. 16) 1943.

12. Coblentz, W. W.: The Physical Aspects of Ultraviolet Radiation in Vitamin-D Therapy, in The Vitamins, Chicago, American Medical Association, 1939, pp. 541-554; J. A. M. A. **111**: 419-423 (July 30) 1938. See extensive bibliography.

13. Bachem, A.: Ultraviolet Action Spectra, Federation Proc. **6**: 71 (March, pt. 2) 1947.

14. Such lamps, in quartz, generate an objectionable amount of ozone.

excessive doses of ultraviolet used to incite cancer of the skin, that hazard seems potential.

It is not my desire to belittle the fact that ultraviolet radiation of wavelengths 2,900 to 3,200 angstroms can be an inciting agent, an irritant, when too frequently applied to the skin in excessive doses. I agree with Blum [15] that, while it is unwise to apply to man these findings of cancer of the skin produced on laboratory animals, it is also unwise to minimize the possibility that cancer of the human skin may result from excessive ultraviolet irradiation.

However, ultraviolet lamps and so-called sunlamps have been in indiscriminate use for over two decades; and if there is a latent period in the development of cancer of the skin, no published reports seem to be forthcoming to indicate that irradiation with such lamps, long ago, was the initial cause. Now that more is known about dosage this potential hazard should become less, as it no doubt will with the increasing indifference to high pressure sales promotion of sunlamps and the waning fad of excessive sun bathing.

Council on Foods and Nutrition

This paper, prepared at the request of the Council on Foods and Nutrition, is one of a series which will appear in THE JOURNAL. The entire series will appear later in book form as the Council's Handbook of Nutrition.

JAMES R. WILSON, M.D., *Secretary.*

FOODS OF PLANT ORIGIN

LEONARD A. MAYNARD, Ph.D.
and
WALTER L. NELSON, Ph.D.
Ithaca, N. Y.

Over 50 per cent of the American diet consists of foods of plant origin. Indirectly as foods for animals, plant products make an additional contribution to the human diet through their influence on the nutritive value of animal products.

In discussing nutritive values, it is necessary to make use of certain average figures for nutrient composition. Foods of plant origin are subject to rather wide variations in composition as influenced by genetic, soil and climatic factors. It is beyond the scope of this article to consider these factors. Their importance is illustrated by the reports of a number of investigators.[1] Some of the factors influencing mineral composition have been reviewed by Beeson.[2] Fortunately the consumer seldom gets his supply of a given food from a single agricultural source, and thus the significance of the wide variation in the composition of crops differently produced is not nearly so great as the individual values might suggest. There are also variations in foods as consumed caused by processing, storage and cooking factors. In the present article attention is called to these factors if they have a particular bearing on the significance of the average values cited. For convenience of discussion, the foods of plant origin are grouped as follows: cereals; legumes and nuts, potatoes, other root crops, tomatoes, leafy vegetables, miscellaneous vegetables, fruits, sugar, syrups and molasses and vegetable oils.

CEREALS

Under cereals are included the cereal grains and their products, including flour, bread, breakfast foods, crackers, cookies, pastry and macaroni. Because of the low cost of cereals in relation to most other foods, their consumption is largest among the low income groups. The importance of these foods in the diet has been set forth editorially in THE JOURNAL [3] as follows:

> The cereal grains are the backbone of the nutrition of most of the races of the earth. They are, as a rule, the cheapest sources of food fuel; so that corn, wheat, rice, rye, barley and oat kernels are to be found constituting a third or often much more of the calory intake of the millions of persons involved.

Cereals also provide a third or more of the protein of the American diet. While this protein is not so high in biologic value as that of animal products, combinations of cereal and animal protein provide a diet of excellent protein quality. Important amounts of phosphorus, iron, copper and other minerals and of certain vitamins are supplied by cereals. Generalizations here are of limited value, however, because of the differences among cereals and the losses which result from milling.

Wheat.—Wheat is by far the leading cereal in the diet in the United States, furnishing approximately 25 per cent of the total calories consumed. The total per capita consumption of flour for 1945 is estimated at 164 pounds (74 Kg.), 97 per cent of which was the milled product, leaving less than 5 pounds (2 Kg.) as whole wheat or graham flour. The consumption of wheat breakfast foods approximated 1½ pounds (0.7 Kg.) per capita. The proximate composition of the flours, as listed by Chatfield and Adams,[4] is presented in table 1.

TABLE 1.—*Proximate Composition of Whole Wheat and of White Flour*

	Protein, Percentage	Fat, Percentage	Carbohydrates, Percentage	Crude Fiber, Percentage
Wheat flour, graham.....	13.0	2.0	72.4	1.8
Wheat flour, patent.....	10.8	0.9	75.9	0.3

It is clear that wheat makes a substantial contribution to the protein needs of the diet. Using the percentage figure for patent flour, one may calculate that the average daily consumption of 6.8 ounces (225 Gm.) of flour supplies 22 Gm. of protein daily, or nearly one third the daily allowance. Whole wheat contains more protein than white flour, and its protein has a higher biologic value, but when white flour is supplemented with milk, eggs or meat a protein mixture of high biologic value results. The much lower fiber content of patent flour reflects the removal of the bran in milling. While bran contributes laxative qualities to the diet, it is poorly digested and may be somewhat irritating to the mucous membranes of the digestive tract. The physiologic effects of bran have been reviewed by the Council on Foods and Nutrition.[5]

15. Blum, H. F.: Photodynamic Action and Diseases Caused by Light, New York, Reinhold Publishing Corporation, 1941, p. 254.

1. Chatfield, C., and Adams, G.: Food Composition, in Food and Life: Yearbook of Agriculture, Washington, D. C., Government Printing Office, 1939, p. 272. Hamner, K. C., and Maynard, L. A.: Factors Influencing the Nutritive Value of the Tomato, Miscellaneous Publication 502, United States Department of Agriculture, 1942. Scott, G. C., and Belkengren, R. O.: Importance of Breeding Peas and Corn for Nutritional Quality, Food Research 9: 371 (Sept.-Oct.) 1944.

2. Beeson, K. C.: The Mineral Composition of Crops with Particular Reference to the Soils in Which They Are Grown, Miscellaneous Bulletin 369, United States Department of Agriculture, March 1941.

3. The Cereals in Nutrition, editorial, J. A. M. A. 95: 1101 (Oct. 11) 1930.

4. Chatfield, C., and Adams: Proximate Composition of American Food Materials, Circular 549, United States Department of Agriculture, June 1940.

5. The Nutritional Significance of Bran, report of the Council on Foods, J. A. M. A. 107: 874 (Sept. 12) 1936.

Several reports [6] have indicated that the calcium, phosphorus and iron of whole wheat flour are poorly utilized and therefore the higher concentration of these nutritents in the whole wheat flours are for the most part an apparent and not a real benefit.

In table 2 are presented the vitamin and mineral values of whole wheat and white flour and, for comparative purposes, the enrichment levels of white patent flour. These levels are based on recommendations of the National Research Council and were compulsory under War Food Order No. 1 of the Federal Security Administration until Oct. 25, 1946. At present (1947) these levels are required by legislation in nineteen states and Puerto Rico and Hawaii. The values for thiamine, riboflavin, nicotinic acid and iron are taken from Tables of Food Composition.[7] Those for pantothenic acid and pyridoxine were supplied by Elvehjem.[8]

The large milling losses of vitamins and minerals are evident from this table. The data show that the outstanding superiority of enriched flour over ordinary white flour lies in its sixfold increase in thiamine content, the figure being 75 per cent of that for whole wheat flour. The data show that milling results in a 60 per cent loss of pantothenic acid and a 50 per cent loss of pyridoxine. Much of the phosphorus and certain other minerals are also lost.

The enriched flour now on the market is nearly all produced by adding the nutrients in question to the refined product. A somewhat similar product can be achieved by "longer extraction" in milling, that is, by retaining some of the vitamin and mineral rich portions of the wheat which are milled out in making patent flour. This is the procedure officially adopted in Canada, as described by Newman.[9]

Wheat flour is consumed to a large extent in the form of bread, of which 85 per cent is commercially baked. Most of this bread is made from white flour, but it is estimated that a majority of the bread now consumed is the enriched product. This enriched bread is obtained either by the use of enriched flour or by the direct addition of the specified minerals and vitamins to the dough.

An important factor in the nutritive value of bread is the extent to which nonfat dry milk solids are used in its manufacture. Six per cent of these is frequently mentioned as the desirable amount in modern bread, but apparently much bread is made with 3 per cent or even less when the cost of nonfat dry milk solids is high. Whole wheat bread is commonly made without milk solids. The inclusion of 6 per cent of the solids increases the calcium content of white bread four times and the phosphorus content twice and adds 0.06 mg. of thiamine and 0.36 mg. of riboflavin per pound. It also improves the protein value considerably. Several reports [10] have appeared showing the improvement in the protein value of white bread made with milk solids when 3 to 5 per cent of soybean flour or 1 to 3 per cent of a cultured food yeast replaced a corresponding amount of the wheat flour used in baking.

The proposed minimum standards for enriched bread which are now being followed are, per pound: thiamine 1.1 mg., riboflavin 0.7 mg., nicotinic acid 10 mg. and iron 8 mg. A similar content of nonfat dry milk solids being assumed, the thiamine content is approximately three times as large as that of ordinary bread, the iron content is increased four times and the nicotinic acid content three times. In other nutrients the enriched product falls somewhat short of whole wheat bread.

TABLE 2.—*Vitamin and Mineral Content of Flours*

	Whole Wheat Flour, Mg./Lb.	White Flour, Mg./Lb.	Enriched Flour,* Mg./Lb.
Thiamine	2.53	0.30	2.0
Riboflavin	0.56	0.15	1.2
Nicotinic acid	25.30	3.50	16.0
Iron	17.3	3.0	13.0
Pantothenic acid	6.03	2.50	
Pyridoxine	2.09	0.99	

* Minimum enrichment levels.

Since whole wheat bread contains the bran which is largely absent in white or in enriched bread, the question of relative digestibility is an important one. This question was thoroughly studied by Rubner [11] during World War I. He found that the advantage of the higher protein content of the unmilled product was offset by its lower digestibility and that it contained slightly less total available calories. Noteworthy modern studies have been published by Murlin and his associates.[12] The first study shows that whole wheat bread has in general a lower protein digestibility value but a higher protein biologic value. The second study reveals no significant differences in the digestibility of the carbohydrates of the two breads. The authors point out that any differences in protein or in available energy values are small and of little importance as compared with differences in vitamins and minerals.

Corn.—Corn meal is the chief form in which corn is used as human food, representing a per capita consumption of 23.4 pounds (11 Kg.) in 1939. An additional 8 pounds (4 Kg.) is consumed as breakfast foods, grits, hominy and canned corn.

The corn grain is approximately equal to the wheat grain in thiamine content but contains only one fourth as much nicotinic acid. It is a good source of phosphorus and iron and certain other minerals. But much of the corn meal and flour consumed, as well as the hominy, grits and breakfast foods, is in the form of milled products. The milling process removes the germ and the bran and thus takes out most of the

6. McCance, R. A., and Widdowson, E. M.: Mineral Metabolism of Healthy Adults on White and Brown Bread Dietaries, J. Physiol. **101**: 44 (June) 1942. Pringle, W. J. S., and Moran, T.: Phytic Acid and Its Destruction in Baking, J. Soc. Chem. Indust. **61**: 108, 1942. Widdowson, E., and McCance, R. A.: Iron Exchanges of Adults on White and Brown Bread Diets, Lancet **1**: 588 (May 16) 1942.

7. Tables of Food Composition, Miscellaneous Publication 572, United States Department of Agriculture, 1945.

8. Teply, L. J.; Strong, F. M., and Elvehjem, C. A.: Nicotinic Acid, Pantothenic Acid and Pyridoxine in Wheat and Wheat Products, J. Nutrition **24**: 167, 1942.

9. Newman, L. H.: The Retention of B Vitamins in Flour and Bread, J. Am. Soc. Agronomy **34**: 109 (Feb.) 1942.

10. Harris, R. S.; Clark, M., and Lockhart, E. E.: Nutritional Value of Bread Containing Soy Flour and Milk Solids, Arch. Biochem. **4**: 243 (May) 1944. Volz, F.; Forbes, R. M.; Nelson, W. L., and Loosli, J. K.: The Effect of Soy Flour on the Nutritive Value of the Protein of White Bread, J. Nutrition **29**: 269 (April) 1945. Sure, B.: Nutritional Improvement of Cereal Flours and Cereal Grains, J. Am. Dietet. A. **22**: 494 (June) 1946.

11. Rubner, M.: Die Verdaulichkeit von Weizenbrot, Arch. f. Anat. u. Physiol., 1916, p. 61.

12. Murlin, J. R.; Marshall, M. E., and Kochakian, C. D.: Digestibility and Biological Value of Whole Wheat-Breads as Compared with White Bread, J. Nutrition **22**: 573 (Dec.) 1941. Sealock, R. R.; Basinski, D. H., and Murlin, J. R.: Apparent Digestibility of Carbohydrates, Fats and "Indigestible Residue" in Whole Wheat and White Breads, ibid. **22**: 589 (Dec.) 1941.

thiamine and minerals present in the entire kernel. The Food and Drug Administration,[13] however, has set standards for enriched corn meal and grits entering interstate commerce which require that each pound contain not less than 2.0 mg. and not more than 3.0 mg. of thiamine, not less than 1.2 mg. and not more than 1.8 mg. of riboflavin, not less than 16 mg. and not more than 24 mg. of nicotinic acid or nicotinamide, and not less than 13 and not more than 26 mg. of iron. North Carolina, South Carolina, Georgia, Alabama and Mississippi have compulsory legislation (1947) which requires that all degermed corn meal and grits sold in the state meet these requirements. These products contain 8 to 9 per cent of protein, which ranks below wheat in biologic value but which combines with milk to provide a protein mixture of high quality. Elvehjem[14] has recently reviewed the role of corn in pellagra-producing diets. The special reason for enriching corn with nicotinic acid is based on the fact that this cereal is used by certain groups in diets which, as a whole, are low in protein and specifically the amino acid tryptophane. Nicotinic acid can serve to decrease the requirement for tryptophane. Inasmuch as corn is low in both tryptophane and nicotinic acid, it is evident that more nicotinic acid is required. Yellow corn meal differs from the white variety, as well as from other cereals, in containing a significant amount of vitamin A: 350 to 500 international units per hundred grams. In view of the rather large consumption of corn meal and other milled corn products by certain groups of the population, the wider use of the unmilled or enriched meal or the development of milling methods which would retain nutrients now lost would be highly desirable.

Canned corn is equal to corn meal in energy and protein on an equivalent moisture basis and is superior to the milled product in mineral and thiamine content.

Oats.—Among the breakfast food cereals, oatmeal and rolled oats, the principal forms in which oats are consumed, rank first both in quantity eaten and in nutritive value. Approximately 529 million pounds (240 million Kg.) are consumed annually. In the milling of oats, only the fibrous hull and the adhering portions are removed, the germ and the other vitamin-rich and mineral-rich portions being left with the product used for human food. Thus oatmeal ranks nutritionally as a whole grain cereal rather than as a milled product.

Oat cereals rank above wheat products both in fuel value and in protein content. Their higher fuel value is due primarily to their fat content (7.4 per cent). Their protein content, over 14 per cent, outranks that of white wheat flour in biologic value. Both oatmeal and rolled oats are low in crude fiber and when properly cooked are highly digestible.

Oatmeal is considerably richer than whole wheat in thiamine. Aughey and Daniel[15] reported that one hundred and twenty minutes' cooking in a double boiler did not cause any appreciable loss of thiamine from rolled oats. The following values for the various vitamins have been reported[7] for uncooked oatmeal: thiamine 2.5 mg. per pound, riboflavin 0.63 mg. per pound and nicotinic acid 5.0 mg. per pound.

Oatmeal is a rich source of iron (23.4 mg. per pound). Its phosphorus content, 66 per cent of which is in the form of phytin, is similar to that of whole wheat.

Rice.—Rice supplies slightly more than 1 per cent of the calories of the average American diet, the annual per capita consumption being approximately 5 pounds (2 Kg.). White, or milled, rice, the form in which most of the consumption occurs, is essentially an energy food. The protein content is around 7.5 per cent, thus being lower than that of corn. Over 50 per cent of the minerals and 85 per cent of the thiamine of the entire kernel are lost in milling. In contrast, brown rice, the product that results when only the hull is removed, contains 0.7 to 0.9 mg. of thiamine per hundred grams. It is nutritionally superior in other respects also. A change from white to lightly milled rice would certainly be in the interests of better nutrition.

Recent developments in the nutritional improvement of white rice have been described by Kik and Williams.[16] Several processes have been proposed for the preparation of milled rice with improved retention of the various vitamins. A comparison of white rice prepared by the conversion process with that of raw rice is given in table 3. It can be seen that a high percentage of the vitamins are retained in the milled product when the conversion process is used.

TABLE 3.—*Thiamine, Riboflavin and Nicotinic Acid Content of Rice*

Type of Rice	Thiamine, Mg./Lb.	Riboflavin, Mg./Lb.	Nicotinic Acid, Mg./Lb.
Rough (brown)	1.48	0.28	26.6
Converted (milled)	1.36	0.20	20.7
Raw (milled)	0.20	0.08	8.3

Rye.—The consumption of rye, mostly as milled rye flour in bread, is less than 3 pounds (1.3 Kg.) per capita annually. This flour is similar to white wheat flour in energy and in protein content. The whole grain contains approximately 2.1 mg. of thiamine per pound, 0.95 mg. of riboflavin and 7.7 mg. of nicotinic acid. Although some of the vitamins are lost when rye flour is degerminated and bleached it is still a better source of most of the B complex factors than white wheat flour.

Barley.—A small amount of barley is consumed as pearl barley and as barley flour for infant feeding. These are milled products which are apparently similar to white wheat flour in energy value but lower in protein content. Milling removes minerals and vitamins to an extent similar to that in the case of wheat.

LEGUMES AND NUTS

Dry legume seeds, such as beans, peas and lentils, are approximately twice as rich in protein as the cereals. While most legume proteins are of rather low biologic value when fed alone, their deficiencies are made up by other proteins in a mixed diet. Dried beans, either home cooked or canned, are noteworthy as a cheap source of protein even though the digestibility is somewhat less than for protein from many other sources.

Dried navy and kidney beans, green or dried lima beans, green or dried peas, lentils and cow peas are all rich sources of thiamine, containing around 0.5 mg. per hundred grams of the dried seed. A part of this thiamine is lost, however, in the cooking process. Two thirds of a cup of baked, canned beans should nevertheless supply one eighth of the day's thiamine requirement. These

13. Enriched Corn Meal and Grits, Food and Drug Administration, Federal Register, May 7, 1947, p. 3112

14. Elvehjem, C. A.: Corn and Pellagra, in Conference on Corn Enrichment, Clemson, S. C., Clemson Agricultural College, July 1947.

15. Aughey, E., and Daniel, E. P.: Effect of Cooking on the Thiamine Content of Foods, J. Nutrition 19: 285 (March) 1940.

16. Kik, M. C., and Williams, R. R.: The Nutritional Improvement of White Rice, Bulletin 112, National Research Council, June 1945.

legumes also supply significant amounts of riboflavin. Fresh green lima beans and peas are rich in ascorbic acid, but a large loss is involved in cooking. The legume seeds are noteworthy also for their iron content, the dried products containing from 6 to 10 mg. per hundred grams. Two thirds of a cup of baked beans will supply one half the daily adult allowance. Legume seeds are notably higher in calcium and in phosphorus than are even the whole cereal seeds.

It is evident that a larger consumption of dried legumes, particularly in place of refined cereals, would improve the diet in several respects. Their cheapness commends them especially for use in low cost diets.

Green and yellow string and wax beans, classed as seed pods, are comparable to the legume seeds in protein, minerals and thiamine per unit of dry matter and in addition contain notable amounts of vitamin A, riboflavin and ascorbic acid.

Peanuts have nutritive values similar to those of the other legumes. They have a much higher energy value due to the high fat content (44 per cent), and the protein is of high biologic value. Peanut butter has a nutritive value similar to that of peanuts. Soybeans are nutritionally similar to peanuts. They are little used as human food in this country. Walnuts are comparable to peanuts in thiamine content, but almonds have somewhat less. All have a high fat and a high protein content and are comparable as sources of calcium and phosphorus.

VEGETABLES

Under the heading "vegetables" are grouped a great variety of foods which differ widely in their nutritive values.

Potatoes.—According to statistics of the United States Department of Agriculture, approximately 275,000,000 bushels of white or Irish potatoes are consumed in the United States per year, or approximately 125 pounds (57 Kg.) per capita. Thus, potatoes provide approximately 4 per cent of the total calory needs on the average. For many persons, however, particularly the lower income groups, potatoes make up a much larger part of the diet than this average figure indicates, and their nutritive value is of added concern accordingly.

Potatoes are primarily an energy food, consisting largely of starch. Approximately 10 per cent of the total calories are in the form of protein of good biologic value. The potato is low in fiber, and according to various investigators it is highly digestible (92 to 99 per cent). It is a significant source of iron, in that one medium-sized potato may provide as much as one tenth of the daily requirement.

As harvested, potatoes contain 12 to 35 mg. of ascorbic acid per hundred grams and thus provide a substantial amount of this vitamin. There is a continuous loss in storage, however, which amounts to 50 to 70 per cent in twelve months. The initial loss is rapid. There is a further loss in cooking, ranging from 14 to 66 per cent according to the procedure, as reported by Esselen and co-workers.[17]

The thiamine content of the potato ranges from 95 to 165 micrograms per hundred grams, which would mean from 8 to 14 per cent of the adult daily requirement in a 150 Gm. serving (approximately the average daily consumption) if it were not for cooking losses. The potato does not supply a significant amount of riboflavin. Iron is richest in the outer portions of the potato; vitamin C seems to be evenly distributed throughout. There is evidence that the vitamin and mineral loss is less in potatoes boiled with the skins on than when baked, but the loss is greatest for peeled potatoes.

The consumption of sweet potatoes in pounds is only about 25 per cent that of the white variety previously discussed. However, per unit weight it contributes appreciably more calories, owing to the higher dry matter content of the sweet variety. Like the white, the sweet potato is primarily an energy food, low in fiber and highly digestible. Only 6 per cent of the total calories are in the form of protein, as compared with 10 per cent for the white variety.

Sweet potatoes are especially noteworthy, however, for their vitamin A value (7,700 international units per hundred grams[7]). Thus, an average-sized serving would supply more than the adult daily allowance of 5,000 international units.[18] Sweet potatoes are apparently similar to white in vitamin C content but lower in thiamine. They are also lower in iron and make no significant contribution to the diet as regards other minerals, except possibly in certain trace elements. An excellent study of the nutritive value of dehydrated sweet potatoes has been published by Lease and Mitchell.[19]

Other Root Crops.—Among other root crops the carrot is high in carotene content. Converting the carotene into international units of vitamin A the values range from 2,200 to 10,000 units per hundred grams, so that approximately three fourths of a cup of cooked carrots should furnish one half to more than two times the daily adult allowance. However, there is some question as to how carotene from various sources is utilized by the body. Utilization values as low as 1 to 19 per cent for man have been reported in the literature.

Compared with the carrot on a calory basis, turnips furnish similar amounts of thiamine, riboflavin, iron and protein, 50 per cent more calcium and eight times as much vitamin C. Swede juice has been reported one half as rich as orange juice. One half a cup of properly cooked turnips should supply approximately one fifth the adult daily allowance of ascorbic acid. Beets are similar to carrots as regards riboflavin and vitamin C content and contain more iron and protein. Raw onions are also a good source of vitamin C,[7] but storage losses range from 14 to 50 per cent, and thus old onions are not a reliable source.

Tomatoes.—Tomatoes are important both because of their special nutritive values and because of their widespread production. They rank third in quantity among the vegetable crops, being exceeded only by white and sweet potatoes. Among the canned vegetables, the tomato in its various forms ranks first.

Tomatoes are outstanding as a source of ascorbic acid, having an average content of 25 mg. per hundred grams for the summer grown products. Thus one small tomato will supply about one third the recommended daily allowance for the adult (75 mg.). The acidity of

17. Esselen, W. B.; Lyons, M. E., and Fellers, C. A.: The Composition and Nutritive Value of Potatoes, with Special Emphasis on Vitamin C, Bulletin 390, Massachusetts Agricultural Experimental Station, March 1942.

18. In setting up this allowance, it was recognized that somewhat more would be required if all the units were furnished as carotene and somewhat less if all were furnished by vitamin A itself, because a unit in the form of carotene may be, under certain conditions at least, only about half as effective in human nutrition as a unit of vitamin A itself. Thus, the rating here given for sweet potatoes, while accurate for comparison with other plant sources of vitamin A, overrates the vegetable in comparison with a source of vitamin A itself. The same considerations apply to later discussions of the vitamin A value of the foods included in this paper.

19. Lease, E. J., and Mitchell, J. H.: Biochemical and Nutritional Studies of Dehydrated Sweet Potato, Bulletin 329, South Carolina Agricultural Experiment Station, June 1940.

the tomato protects it against any considerable loss in cooking. In the canning of tomatoes and tomato juice there is little loss of the vitamin if the process is properly carried out. However, tomato juice purchased on the retail market has been shown to vary considerably in ascorbic acid content. Values ranging from 2.5 mg. to 25.2 mg. per hundred grams have been reported. One 5 ounce (150 cc.) glass of tomato juice supplies about one third the daily allowance. Recent evidence indicates that tomatoes as purchased on the northern markets in winter contain much less ascorbic acid than those available in summer.

Tomatoes are also rich in carotene. Ripe tomatoes, fresh or canned, contain approximately 1,000 international units of vitamin A per hundred grams. This means that one small tomato or a 5 ounce glass of canned juice will supply about one fifth the daily adult allowance.

On the basis of the available figures, tomatoes in the amounts consumed cannot be considered as an important source of any of the B group of vitamins or of the mineral elements with the possible exception of iron.

Leafy Vegetables.—The leafy vegetables, including cabbage, kale, chard, broccoli, spinach, turnip greens, collards, lettuce and beet greens, are outstanding sources of certain minerals and vitamins. They are particularly noteworthy for their calcium, the important element in which cereals, potatoes and most other foods except milk and cheese are deficient. Among the leafy vegetables mentioned, turnip greens rank at the top in calcium content. One half cup (3 ounces, or 90 cc.) of the cooked greens will supply approximately one third the daily adult allowance. Broccoli, collards, kale, loose leaf lettuce and mustard greens are also rich sources. Head lettuce and cabbage are relatively low, but cabbage greens and the outer leaves of cabbage rank even higher than turnip greens.

Experiments by Fincke [20] have shown that the calcium content of broccoli and that of cauliflower are nearly as available as that of milk. Speirs [21] has reported that the utilization of calcium from turnip greens is about equal to that from milk but that the calcium in tender greens, collards and kale is less well utilized. The calcium of spinach, beet greens, chard and lamb's-quarters is not nutritionally available because of the high oxalic content of these vegetables.

The calcium contribution of green leafy vegetables becomes particularly important in diets containing little milk or cheese.

The green leafy vegetables are important sources of iron. A serving (3 ounces) of cooked turnip greens, mustard greens, spinach, chard or beet greens will supply approximately 25 per cent of the adult daily allowance. Kale supplies somewhat less and headed lettuce and cabbage are relatively poor sources.

The green leafy vegetables are all rich sources of carotene and thus make an important contribution to the vitamin A content of the diet. A range of 2,800 to 13,650 international units per hundred grams for kale, chard, spinach, turnip greens, dandelion greens and mustard greens has been reported.[7] The greener and leafier the product, the higher is the vitamin A content. Carotene from green leafy vegetables seems to be better utilized than that from the yellow vegetables. Allowing for losses in cooking and for the fact that the vitamin allowance must be higher when carotene is the source, a 3 ounce serving of one of these greens can be relied on approximately to meet the day's needs. Headed cabbage and lettuce are relatively poor sources.

In the fresh state, the leafy vegetables are excellent sources of vitamin C. A cup of raw shredded cabbage will furnish nearly a third of the day's allowance. Watercress, collards, broccoli, turnip greens, mustard greens and kale are similar in vitamin C content to cabbage; beet greens and dandelion greens contain somewhat less; lettuce, escarole and endive contain much less. Leafy vegetables lose vitamin C by oxidation in storage and also in cooking. Further losses occur by solution in cooking if the cooking water is discarded. Gould, Tressler and King [22] found that, in cooking, 25 per cent of the vitamin C of cabbage was destroyed by oxidation and another 25 per cent lost in the cooking water. Other vegetables have shown similar losses. In the preparation of vegetables, further destruction of vitamin C by oxidation occurs when they are crushed or bruised or allowed to stand for long periods of time at room temperature both before and after cooking. Cutting and chopping into small pieces also accelerates the oxidation of vitamin C but in order to reduce the cooking time it is sometimes advisable to do this with large vegetables, particularly if they are cooked in very small amounts of water. Vitamin C losses can be decreased by refrigerating the vegetables until ready to prepare and serve. In cooking use as little water as possible, have the water boiling to start with, bring the water back to the boil quickly after adding the vegetables and keep the cooking time at a minimum. The same methods which help to conserve the vitamin C value will also conserve riboflavin, thiamine and mineral values. All these food components are more or less soluble in water.

Most of the green leafy vegetables are excellent sources of riboflavin, the leaves being much richer than the stems. A serving of cooked beet greens will supply about one fourth of the daily adult allowance. Spinach and kale supply about one fifth. Other greens supply a lesser amount, headed cabbage and lettuce ranking at the bottom of the list. Leafy vegetables are not a good source of thiamine, furnishing only 3 to 15 per cent of the adult daily allowance. The destruction in cooking usually does not exceed 10 to 15 per cent, and when large amounts of water are used and discarded, large additional losses occur by solution. Certain leafy vegetables have been found effective in preventing and curing pellagra. The following values have been reported for some of the green vegetables (mg. per hundred grams) : spinach 0.70, broccoli 0.90, cress 1.0 to 2.0 and kale 2.0.

In the amounts commonly consumed, leafy vegetables are of little significance as energy foods, but their higher carbohydrate content provides roughage, which is needed in certain diets. They are relatively richer in protein than in calories, and their protein ranks above seed proteins in general in biologic value. However, the actual contribution to the diet in the amounts commonly consumed is small.

Miscellaneous Vegetables.—There are several other vegetables which, although limited as to general use, make important contributions to the diet of certain groups. The Hubbard, or winter, variety of yellow squash contains 5,000 international units of vitamin A per hundred grams. One half cup of the cooked product

20. Fincke, M. L.: The Utilization of the Calcium of Cauliflower and Broccoli, J. Nutrition **22**: 477 (Nov.) 1941.

21. Speirs, M.: The Utilization of Calcium in Various Greens, J. Nutrition **17**: 557 (June) 1939.

22. Gould, S.; Tressler, D. K., and King, C. G.: Vitamin C Content of Vegetables: V. Cabbage, Food Research **1**: 427 (Sept.-Oct.) 1936.

supplies nearly one half the adult daily allowance. Summer squash contains much less. Pumpkin furnishes approximately one fourth as much as winter squash.

A serving of fresh asparagus (nonbleached) can furnish approximately one seventh the day's allowance of vitamin A and one sixth that of vitamin C. It is also a significant source of calcium and iron. Brussel sprouts are rich sources of vitamin C and also furnish significant amounts of iron, calcium and vitamin A. Cauliflower is notable for its content of ascorbic acid, thiamine and riboflavin.

One medium-sized sweet pepper will furnish 630 international units of vitamin A and 180 to 200 mg. of vitamin C. Chili peppers, whether fresh or dried, are a good source of vitamin A. Fresh chili is an excellent source of vitamin C. Some of the vitamin C is retained on canning. Okra contains 740 international units of vitamin A per hundred grams. Parsley, which is used mainly for decoration, is an excellent source of both vitamin A and iron. When fresh it furnishes some vitamin C.

FRUITS

According to United States Department of Agriculture statistics, the approximate per capita consumption of fruits, calculated on the fresh basis, is about 150 pounds (68 Kg.). Of this total, 75 per cent is consumed fresh and 15 per cent canned, and the remainder is divided between dried fruits and juices. Apples outranked all other fruits, representing over one fourth the total consumption. But citrus fruits as a class exceed apples by 50 per cent or more. The nutritive values of various fruits have been excellently summarized in an article by Morgan,[23] and we have drawn on this article for many of the data which follow.

Fruits do not contribute important amounts of either calories or proteins to the diet, but they are of outstanding value because of their content of certain vitamins and minerals. As a class, fruits are important sources of ascorbic acid, certain members of the B complex, vitamin A, iron and other minerals, but there is a large variation among the different kinds as regards the extent of their contributions.

The citrus fruits are especially important for their ascorbic acid content. A medium-sized orange weighing about 5½ ounces (155 Gm.) will meet the daily adult allowance. A somewhat greater weight of grapefruit is required. Four and one-half ounces (130 Gm.) of canned orange or lemon juice or 6 ounces (170 Gm.) of canned grapefruit juice would supply the daily allowance. While the citrus fruits cannot be considered important sources of other nutrients, they do contain iron, calcium and thiamine in amounts which are of some significance in the diet. Pineapples, which are consumed mostly canned or as juice, contain about half as much vitamin C as do citrus fruits and are in general similar in other values.

Apricots and yellow peaches are important sources of vitamin A. The day's adult allowance is supplied by 3½ ounces (100 Gm.) of fresh or canned apricots or by approximately three times as much fresh or canned peaches. Weight for weight, dried peaches and dried apricots supply approximately three times as much vitamin A as the fresh products. Cantaloupes contain about half as much of this vitamin as do fresh peaches, and they are an important source of ascorbic acid, being about equal to the citrus fruits. Dried prunes furnish significant amounts of vitamin A, riboflavin and thiamine. Plums rank above other fresh fruits in thiamine content. Apricots, peaches and to a lesser extent prunes are significant sources of iron.

Apples cannot be considered a large source of any vitamin or mineral nutrient. In view of their large consumption, however, they do make a significant contribution of ascorbic acid to the diet. A medium-sized apple weighing 6 ounces supplies on the average about one tenth the day's allowance, but there are decided differences among varieties. The keeping qualities of apples make it possible for them to be marketed throughout the winter in latitudes where fresh grown sources of vitamins are unavailable or high in price. In rural areas in which they are produced, home-stored apples undoubtedly make an important contribution of ascorbic acid to the diet during the winter season, when the problem of getting adequate supplies of this vitamin is most difficult. Apples also contain a significant amount of iron. There is a 25 per cent loss of vitamin C in making applesauce. The loss is greater when apples are baked or made into pie.

Bananas are similar to apples in vitamin C value: they contain almost twice the iron. Bananas are a significant source of vitamin A.

Fresh strawberries are another food high in vitamin C, the range for eleven varieties being between 40 to 104 mg. per hundred grams. Thus one-half cup would supply from two thirds to more than the daily need for ascorbic acid.[24]

SUGARS, SYRUPS AND MOLASSES

White sugar contributes only calories to the diet. It is clear that the present large consumption of sugar is disadvantageous in that it means a smaller consumption of nutritionally superior foods. Brown sugar, corn syrup, honey, maple syrup and maple sugar contain small amounts of calcium and iron. Honey contains small amounts of some of the B vitamins and vitamin C. Molasses is an excellent source of both, 1½ tablespoons furnishing approximately one tenth the estimated daily adult allowance of calcium and one fifth the estimated daily adult need of iron. Sorghum supplies a lesser amount of calcium and about an equal amount of iron. Table blend syrups contain a significant but lesser amount of iron.

VEGETABLE OILS

Cottonseed, corn, soybean, peanut and olive oils and in lesser amounts other vegetable oils are consumed as shortenings, salad oils and margarines. The oils as such are sources only of energy and essential fatty acids. Many oleomargarines are now fortified with 15,000 international units of vitamin A per pound; they may also supply some vitamin D.

Tuberculosis Control.—Minimal, noninfectious cases of tuberculosis are private physicians' cases, not sanatorium cases. Indeed, the private practitioner can be a major force in the future control of tuberculosis in the communities of our country if he undertakes to participate in follow-up activities after surveys have been completed. Through his efforts, minimal tuberculosis can be checked and, in individual cases, never become serious. Under the physician's care, needless distress and tragedy can be avoided. As a consequence of his vigilance, the general practitioner can reduce the occurrence of deaths from tuberculosis.—Weber, F. J.: *Ohio Public Health*, February 1948.

23. Morgan, A. F.: A Nutritive Index of Fruits, Fruit Products J. 21: 75 (Nov.) 1941.

24. Burkhart, L., and Lineberry, R. A.: Determination of Vitamin C and Its Sampling Variation in Strawberries, Food Research 7: 332 (July-Aug.) 1942.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary*

CHLOROQUINE DIPHOSPHATE.—Aralen Diphosphate-Winthrop. — 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline diphosphate.—$C_{18}H_{32}ClN_3O_8P_2$.—M. W. 515.88.

Actions and Uses.—Chloroquine diphosphate is highly active against the erythrocytic forms of Plasmodium vivax and Plasmodium falciparum. It does not prevent relapses in vivax malaria, nor will it prevent the establishment of vivax infection when administered as a prophylactic. It is, however, effective in vivax malaria as a suppressive agent and for the termination of acute attacks, significantly lengthening the interval between treatment and relapse.

In falciparum malaria, chloroquine diphosphate abolishes the acute attack and effects complete cure of the infection.

Chloroquine diphosphate has approximately three times the activity of quinacrine hydrochloride against standardized strains of P. vivax and P. falciparum.

Chloroquine diphosphate is rapidly and completely absorbed by the gastrointestinal tract. Some of it is excreted slowly in the urine. Considerable amounts are deposited in the organs and tissues, and it is concentrated in nucleated cells, particularly those of the liver, spleen, kidneys and lungs.

Dosage.—Chloroquine diphosphate is usually administered orally either before or after meals. For suppression of vivax malaria a weekly dose of 0.5 Gm. given at exactly seven day intervals is recommended.

Chloroquine diphosphate is metabolized in the body, but this occurs slowly and the drug may be detected in body tissues for more than a week after discontinuing medication. The drug is well tolerated in therapeutic doses and does not produce cinchonism or discolor the skin. However, there may be mild headache, pruritus, visual disturbances and gastrointestinal complaints following therapeutic doses. Blurring of vision and difficulty in focusing are occasionally observed following prolonged administration. None of the side reactions appears serious, and all have been of a reversible nature.

For treatment of acute attacks of malaria due to P. vivax and P. falciparum, an initial dose of 1 Gm. followed by an additional 0.5 Gm. after six to eight hours and a single dose of 0.5 Gm. on each of two consecutive days (total of 2.5 Gm. in three days) is sufficient to eradicate most infections with P. falciparum and to terminate an acute attack of vivax malaria. In the latter, freedom from clinical attacks may be maintained thereafter by administration of suppressive doses (0.5 Gm. weekly).

Tests and Standards.—

Chloroquine diphosphate occurs as a white, crystalline powder possessing a bitter taste. It melts in the range 193 to 195 C. Two modifications of chloroquine diphosphate are obtainable. The second form melts at 215 to 218 C. It is freely soluble in water and practically insoluble in alcohol, benzene, chloroform and ether. The *p*H of a 1 per cent solution is about 4.5.

Dissolve about 50 mg. of chloroquine diphosphate in 3 cc. of water. Add a few drops of ammonium molybdate test solution: a white precipitate develops immediately.

Dissolve 20 mg. of chloroquine diphosphate in 20 cc. of water. Add 5 cc. of a saturated aqueous solution of picric acid: a yellow precipitate forms immediately. Filter off the precipitate, wash with water and air-dry on the filter funnel: the product melts from 205 to 210 C. *(Caution!)*

Dissolve 0.25 Gm. of chloroquine diphosphate in 50 cc. of water. Add 1 cc. of strong ammonia solution and extract with two 30 cc. portions of cyclohexane. Evaporate the cyclohexane solution to dryness on the steam bath. Place the residual oil in a vacuum desiccator over phosphorus pentoxide and allow to stand over night to permit crystallization: the solid material melts at a temperature of 87 to 90 C.

Dry about 0.25 Gm. of chloroquine diphosphate, accurately weighed, in vacuum over phosphorus pentoxide at room temperature for forty-eight hours: the loss in weight does not exceed 2 per cent.

Dissolve about 0.2 Gm. of chloroquine diphosphate, accurately weighed, in 50 cc. of water. Dissolve 1.5 Gm. of bismuth oxynitrate in 10 cc. of nitric acid and dilute to 100 cc. with water. Add 50 cc. of the bismuth solution to the solution of chloroquine diphosphate. Digest for two hours on the steam bath, filter into a tared Gooch crucible and wash with dilute nitric acid (2 cc. to 100 cc.). Wash successively with water, alcohol and ether. Dry in an oven at 100 C. for two hours: the phosphorus content is not less than 11.8 per cent or more than 12.25 per cent.

Weigh, accurately, about 0.2 Gm. of chloroquine diphosphate. Dissolve in 50 cc. of water, transfer to a separatory funnel. Add 5 cc. of ammonium hydroxide and extract with 25, 20, 15, 10 and 10 cc. portions of ether. Drain the combined ether extracts through a cotton pledget into a 100 cc. tared beaker. Evaporate the solution on the steam bath to dryness and finally heat at 100 C. for thirty minutes: the residue, calculated to chloroquine diphosphate, is not less than 98 per cent or more than 102 per cent.

CHLOROQUINE DIPHOSPHATE TABLETS

Grind ten tablets in a mortar. Weigh, accurately, about 0.3 Gm. of the pulverized tablets. Dissolve in about 50 cc. of water, filter and wash the residue with about 20 cc. of water. Transfer to a separatory funnel, add 5 cc. of ammonium hydroxide and extract with 25, 20, 15, 10 and 10 cc. portions of ether. Drain the combined ether extracts through a cotton pledget into a 100 cc. tared beaker. Evaporate the solution on the steam bath to dryness and finally heat at 100 C. for thirty minutes: the residue, calculated to chloroquine diphosphate, is not less than 95 per cent or more than 105 per cent.

WINTHROP-STEARNS, INC., NEW YORK

Tablets Aralen Diphosphate: 0.25 Gm.

U. S. patent 2,233,970 (March 4, 1941; expires 1958).
U. S. trademark registration pending.

ASCORBIC ACID See New and Nonofficial Remedies, 1947, p. 517).

The following additional dosage form has been accepted:

THE NATIONAL DRUG COMPANY, PHILADELPHIA

Tablets Ascorbic Acid: 100 mg.

ESTRONE (See New and Nonofficial Remedies, 1947, p. 341).

The following additional dosage forms have been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Estrone in Oil: 10 cc. vials containing 1 mg. (10,000 international units) in peanut oil. Preserved with 0.5 per cent chlorobutanol.

Aqueous Suspension Estrone: 1 mg. in 1 cc. ampuls (10,000 international units) and 5 mg. in 1 cc. ampuls (50,000 international units). Each cubic centimeter contains estrone crystals in aqueous suspension with isotonic sodium chloride solution, stabilized with acacia.

PERTUSSIS IMMUNE SERUM (Human) (See New and Nonofficial Remedies, 1947, p. 440).

The following dosage form has been accepted:

HYLAND LABORATORIES, LOS ANGELES

Pertussis Immune Serum (Human): Vials containing vacuum-dried powder representing 20 cc. of pertussis immune serum (human) preserved with merthiolate 1:35,000. Each vial is packaged with a 10 cc. vial of sterile distilled water.

NICOTINAMIDE (See New and Nonofficial Remedies, 1947, p. 514).

The following additional dosage form has been accepted:

AMERICAN PHARMACEUTICAL CO., INC., NEW YORK

Tablets Nicotinamide 100 mg.

ESTROGENIC SUBSTANCES (See New and Nonofficial Remedies, 1947, p. 343).

The following dosage forms have been accepted:

GEORGE A. BREON & CO., INC., KANSAS CITY, MO.

Solution Estrogenic Substances in Oil with Chlorobutanol 3 per Cent: 30 cc. vials containing the equivalent of 10,000 international units per cubic centimeter in sesame oil. Preserved with 3 per cent chlorobutanol.

FORBES LABORATORIES, NEW YORK

Solution Estrogenic Substances in Oil: 1 cc. ampuls and 10 cc. and 30 cc. vials containing 10,000 international units and 1 cc. ampuls and 10 cc. and 20 cc. vials containing 20,000 international units in sesame oil. Preserved with 0.5 per cent chlorobutanol.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 17, 1948

HOSPITAL NUMBER POSTPONED

Under normal conditions this issue of THE JOURNAL would be the annual Hospital Number. However, the absence from their work of the compositors employed by the American Medical Association continues, and it is necessary to postpone the Hospital Number until arrangements can be made to set up the large tables of statistics that special number contains. It is hoped this can be done by late May or early June.

BAGASSE DISEASE OF THE LUNGS

Sugar cane from which the juice has been extracted is called bagasse. The product is stored in the open for months or years when it is broken, processed and pressed into various shapes for insulating building materials. The dust of the dried grass is an industrial hazard. The disease that follows its inhalation is known under the dubious name of bagasse or even more improperly, perhaps, as bagassosis[1] or bagasscosis.[2] Sodeman and Pullen[3] state that "Since the suffix 'osis' is properly added only to words formed from Greek roots and since we have as yet not been able to trace the term 'bagasse' to the Greek, we prefer the simple term 'bagasse disease of the lungs."

Bagasse disease of the lungs is characterized by cough, dyspnea and hemoptysis, night sweats, chills and intermittent fever. Roentgenologic examination of the chest shows mottling of both lungs, like that of miliary tuberculosis. The disease commences insidiously. The pulmonary reactions incited by the inhalation of bagasse dust are reversible and complete resolution may occur. Because the disease is seldom fatal, only rare opportunities have thus far been presented to determine the histologic changes in the lungs. Investigations of this sort have been limited to a single necropsy and to the removal of a few particles of tissue for biopsy, The lesions so far described consist of localized pneumonic areas composed of foam cells together with foreign body reactions around bagasse fibers.

The cause of bagasse disease is still obscure. Some investigators believe it is either a fungus or a bacterial infection, the causative agents being introduced on the surface of the inhaled dust. Others contend that it is a virus disease and still others that it is an allergic response to the presence of bagasse material.

Gerstl, Tager and Marinaro[4] have approached the subject experimentally and the results are suggestive. Suspensions of five lots of bagasse were administered intravenously, insufflated into the trachea or injected into the skin of rabbits and guinea pigs. Animals receiving intravenous injections of bagasse in suspension rapidly became ill or died. When, however, the dust was autoclaved similar amounts of the suspension could be given without apparent ill effects. The lungs and other viscera of the animals receiving fresh bagasse suspension showed extensive foci of necrosis and cellular reactions. In addition, the presence of mycelia and spores in the damaged organs served as an indication of the nature of the infective agent. Animals that received injections of autoclaved bagasse revealed only small granulomas in the lungs of the foreign body type. These results suggest that bagasse disease of the lungs is caused by a fungus and that the dust itself is relatively innocuous.

1. Castleden, L.I.M., and Hamilton-Paterson, J.L.: Bagassosis: An Industrial Lung Disease, Brit. M.J. 2: 478, 1942.
2. Jamison, C., and Hopkins, J.: Bagasscosis: A Fungus Disease of the Lung, New Orleans M. & S.J. 93:580, 1941.
3. Sodeman, W.A., and Pullen, R.L.: Bagasse Disease of the Lungs, Arch. Int. Med. 73:365, 1944.
4. Gerstle, B., Tager, M., and Marinaro, N. A., Pathogenicity of Bagasse, Arch. Path. 44: 343, 1947.

THE DEVELOPMENT AND PROGRESS OF NEUROSURGERY

In his centennial address before the Section on Nervous and Mental Diseases of the Annual Session of the American Medical Association at Atlantic City, N.J., June 12, 1947, Stanley Cobb reviewed progress in the previous hundred years in neurology, psychiatry and neurosurgery.[1] In 1847 specialisation in medicine was just beginning. While psychiatry was already developing, neurology was in the earliest stages and neurosurgery did not exist. After

1. Cobb, S.: One Hundred Years of Progress in Neurology, Psychiatry and Neurosurgery, Arch. Neurol. & Psychiat. 59: 63-98 (Jan.) 1948.

instructive sketches of the advances in the knowledge of the nervous system, its structure, physiology and diseases, Cobb considered neurosurgery, which did not begin until about 1900. The technics of neurosurgery—asepsis, anesthesia and hemostasis—were not sufficiently developed earlier, which was the case also with the clinical localization of lesions within the brain and the cord.

According to Cobb, Godlee in 1884 removed the first brain tumor "localized scientifically." Trepanning was done by the neolithic man; Hippocrates used the trephine with occasional success, and by 1890 more and more successful operations were performed on the brain. Sir Victor Horsley (1857–1916) is listed as the first neurosurgical specialist. He devoted his life to neurosurgery, for which he prepared himself by operations on dogs and monkeys. He was a great source of inspiration and added much to the understanding of cerebral physiology. According to present standards his technic seems rather rough and the care that his patients received seems somewhat primitive.

After due mention of other pioneers in neurosurgery, Cobb called special attention to Harvey Cushing (1869–1939), who, besides guiding neurosurgery into a specialty of the first order, advanced greatly the knowledge of brain tumors, their clinical manifestations, their structure and origin, their effects on nervous functions and their surgical treatment. Cushing removed his 2,000th brain tumor in May 1931 and operated for the last time in November 1932.

Neurosurgery has expanded greatly since pioneer days. A notable number of physicians have devoted themselves to the long and difficult training in the technics and the background of neurosurgery. The 1939 meeting of the Harvey Cushing Society was attended by thirty-seven members. According to Cobb two hundred and thirty-one surgeons have been approved by the board of neurosurgery. Frontal leukotomy has increased the understanding of the functions of the frontal areas of the brain, and there seems to be good reason to expect new advances in neurology and psychiatry as neurosurgery extends.

Cobb closed his valuable review with the following paragraph:

> One hundred years from now, when some neurologist of the twenty-first century gives this historical review for the bicentenary of the American Medical Association, he will tell of many advances with the new technics of physics and chemistry. Words we are just learning to use will be commonplace, and new terms and concepts that we could not understand will be used. Our present theories will seem primitive. Nevertheless, the golden years of anatomy in the late nineteenth century will not be forgotten. The resurgence of neurophysiology in the beginning of the twentieth century will remain a great epoch. The development of neurosurgery will stand as an example of hard-earned medical progress by brilliant and courageous men. And, unless we pay more heed to social psychology and to the facts that psychiatry is gleaning from the study of interpersonal relations, there will be no meeting of the American Medical Association in 2047!

Current Comment

HEMOCONCENTRATION AND GASTRIC ULCER

Hemoconcentration following extensive superficial burns was believed by Kapsinow[1] to be the etiologic factor in the production of gastric and duodenal lesions (Curling's ulcer). Friesen and Wangensteen[2] of the Department of Surgery, University of Minnesota Medical School, studied the question by experiments on dogs under deep intravenous sodium pentobarbital anesthesia (15 mg. per pound). In 12 of 14 dogs subjected to burns accompanied by the administration of histamine hemoconcentration developed, the hematocrit reading rising from an average of 44 per cent to an average of 55.7 per cent. Readings as high as 65 to 72 per cent were recorded in certain dogs. All 12 dogs showed congestion of the mucous membrane of the stomach and duodenum. Nine of them showed definite Curling's ulcer, 5 bleeding and 3 perforating. The 2 dogs in which increased concentration of the blood failed to develop did not demonstrate gastric or duodenal abnormality. In a seconed group of dogs subjected to burns accompanied by the administration of histamine in beeswax, attempts were made to prevent hemoconcentration by controlled intravenous instillations of plasma. In all cases in which blood concentration was maintained at a normal level, gastric or duodenal abnormality did not appear. Similar though less pronounced results were obtained in dogs in which increase in gastric secretion was not produced by histamine injection. From these results increased concentration of the blood following extensive superficial burns is the dominant etiologic factor in the production of Curling's ulcer. Gastrointestinal abnormalities following such burns can be prevented by adequate antihemoconcentration therapy.

1. Kapsinow, R.: South. M. J. 27:599, 1934.

2. Friesen, S. R., and Wangensteen, O. H.: Proc. Soc. Exper. Biol. & Med. 64:81, 1947.

Official Notes

AMEND BROADCAST PROGRAM

Due to cancellation of time by the National Broadcasting Company for April 24, the program of the American Medical Association Network series, "Doctors Today," scheduled for that date will be broadcast May 1. Subsequent programs will be broadcast a week later than originally scheduled in the March 27 issue of THE JOURNAL. The amended program is as follows:

May 1, 1948	Child Guidance
May 8, 1948	Health for Every Citizen
May 15, 1948	Human Brucellosis

Washington Letter

(From a Special Correspondent)

April 15, 1948

Scheele Testifies Before Committee

One of the first official acts of Dr. Leonard A. Scheele, following his induction as Surgeon General of the Public Health Service, was to testify before a congressional committee. He told the House Committee on Interstate Commerce that 54,000,000 Americans live in communities which lack full time local health services. In accepting his appointment Dr. Scheele said: "The health of the American people and their health resources cannot and must not become a monopoly, either of governments, private enterprise or charitable organizations. Each of these great institutions has made incalculable contributions to American Health. The constituent groups and organizations within them must endure and grow in wisdom, strength and efficiency."

Outline Plan to Replace Physicians

Dr. Paul Magnuson, medical director of the Veterans Administration, reported that a plan has been worked out to replace the thirteen hundred physicians on loan from the Army and Navy who are expected to leave the agency this summer. Outgoing military physicians will be replaced by three year resident physicians. To assist the agency and simultaneously broaden opportunities for residents, prospective specialists will serve their final two years in veterans' hospitals, practicing under the supervision of certifified consultants. The agency now has a residency program covering the first three years of the specialty apprenticeship. The advanced program will provide salaries from $4,100 to $7,000 annually.

Approves Allowances For Disabled Veteran's Dependents

The House Veterans Committee unanimously approved a bill to give $61,800,000 in special allowances to dependents of 130,700 veterans with disabilities of 60 per cent or more. The bill, if finally approved, would for the first time establish benefits for dependents of disabled men. It would give these allowances to dependents of totally disabled veterans of World Wars I and II: wife, $30 a month; first child, $20; next two children, $15 each; dependent mother or father, $25 each. The allowances would be reduced for lesser disabilities.

Rider To Appropriations Bill Rejected By Committee

Representative Frank Keefe, Republican, Wisconsin, sponsored a civil rights rider to the appropriations bill which would have barred federal public health, hospital and vocational educational grants from states practicing racial discrimination. The defeated Keefe amendment read: "No part of the appropriations provided for in this act shall be paid as grants to any state or educational institution in which, because of race, color or creed, discriminatory practices deny equality of educational opportunity or employment to pursue such educational courses or employment as are provided for by such grant." The rider would have denied federal subsidies from state universities or hospitals that do not admit Negroes. Suspension of the rider is said to have removed another potential source of controversy in the present civil rights issue over which Southern Democrats threaten to withdraw from the party and have taken steps to remove President Truman's name from state ballots.

Experts Say Physicians Are Unprepared For Atomic Attack

In a recent address here, Rear Admiral Clarence J. Brown, assistant chief of the Bureau of Research and Medical Military Specialties, declared that the nation's physicians are unprepared for the emergency of an atomic bomb attack in the event of another war. He advocated that all medical practitioners take training in military aspects of medicine. The general public, he said, "may possibly derive some comfort from the hope that threat of retaliation might minimize an enemy attack." "Not so of the medical profession," he said; "its work begins before any retaliation. Long before the retaliation bombs are received by the enemy, we shall be confronted in our great cities by the world's greatest catastrophe, such utter devastation, such unexampled human misery as transcends the imagination. During the immediate hours and days which follow, who will bear the burden of the professional care of the survivors? Who will set up the sanitary controls, provide the mass innoculations, insure the safety of food and water supplies, and direct the diagnosis and treatment of those who are suffering insidious radiation illness?"

STATE LEGISLATION

Kentucky

Bills Enacted.--H. 447 was approved March 25. Relating to training of Negro nurses and doctors, it provides that nothing in the law shall be construed to prohibit the giving of instruction in nursing, medicine, surgery, or other related courses of graduate grade or on the professional level, within any hospital, if the governing body of the hospital, by a majority vote of its of its members, so elects.

S. 105 was approved March 29. It provides for the creation of a medical research commission to provide for a program of research in the fields of medicine, surgery and allied sciences, preventive medicine, control of diseases and all other features of medicine and surgery that affect the health and welfare of the people of the state.

GOVERNMENT SERVICES

ARMY

NEW PROFESSIONAL TRAINING OPPORTUNITIES

A greatly expanded professional training program for regular and reserve medical officers of the Army has been announced by the Surgeon General. The program calls for one thousand, nine hundred new physicians in the Regular Army and an increasing number of volunteer reserve officers on active duty. It is designed to give many more Army physicians the training to meet requirements for certification by American Specialty Boards, and to further integrate civilian and military medicine. The following five major aspects of the new program were described by the Surgeon General:

1. Physicians already resident in civilian hospitals are now eligible for commissions in the Regular Army. Those commissioned may continue their residencies with full pay and allowances and will be assigned by the Army to the civilian hospital in which they are already resident. Even in the event of a major emergency, residents will complete their training, if it is at all possible. Chances of continuing training for these men will be at least as good as those of civilian physicians in resident training. The Surgeon General's Office will commission three hundred residents under this aspect of the program in 1948, three hundred in 1949-1950 as senior residents, one hundred as residents and a hundred and fifty as junior residents.

2. Civilian interns are now eligible for commissions in the Army medical corps reserve and may continue their internship with full Army pay and allowances. Those so commissioned will undertake to accept a commission in the Regular Army on completion of their internship, and will then be permitted to compete for Army residencies in either Army or civilian hospitals. In 1948 and again in 1949, three hundred interns will be included in this phase of the training program.

3. During 1948, five hundred younger physicians will be commissioned and assigned to duty at Army hospitals in order to compete for two hundred and sixty residencies in both Army and civilian hospitals. Competitive examinations will begin in either September or October, 1948. These residencies are apportioned among the various specialties according to the needs of the Army medical corps. Resignation of officers commissioned under this phase of the program will not be accepted within one year after the date of commission.

4. One hundred and fifty commissions in the grades of major, lieutenant colonel and colonel will be offered in 1948 and an equal number in 1949 to physicians who have completed their training. This aspect of the program is not limited to those men already certified as specialists, since outstanding officers for command and staff positions are needed as well as professional men. Applicants for those commissions in higher grades will not be considered for residencies or specialty training.

5. Active reserve service for specific positions and limited periods will be offered physicians who are not interested in a Regular Army career. Those who come into the service in this manner will not be eligible for residencies, but time spent in practice under this aspect of the program may receive recognition by the specialty boards.

The program is designed to attract to a Regular Army career medical talent of the highest caliber. One year of active duty as distinguished from training duty is expected for each year of training, whether the training is received in Army or civilian institutions. Resignations will not be considered until this obligation has been fulfilled.

Training continuous until completion of the requirements for Specialty Board certification is a definite aim of the program, the Surgeon General emphasized.

The program has been presented to the Council on Medical Education and Hospitals of the American Medical Association and to the Association of American Medical Colleges. Both bodies have officially recognized the value of the program in its entirety.

Information concerning any part of the program may be obtained from the Surgeon General's Office. Address requests to the attention of the Chief of Personnel, Surgeon General's Office, Department of the Army, Washington, D. C.

INSTITUTE OF PATHOLOGY

Members of the staff of the Army Institute of Pathology presented the following papers at the American Association of Pathologists and Bacteriologists and of the International Association of Medical Museums at Philadelphia in March:

Dr. Ira Gore (Veterans Administration), Morphologic Aspects of Disseminated Platelet Thromboses.

Dr. Webb Haymaker, Pathology of Herpes Simplex Encephalitis; Report on Three Proved Cases.

Dr. Lent C. Johnson, Histogenesis of Myositis Ossificans.

Dr. Hans F. Smetana, Histologic Lesions Encountered in Regional Enteritis.

The following lectures or seminars were given by members of the staff during February:

Dr. Elson B. Helwig at Georgetown University, Pigmentation.

Dr. Lent C. Johnson at Arlington Hospital, Va., Recent advances in Nephritis; and before the Alexandria Medical Society, Dynamic Pathology of Eclampsia.

Dr. Webb Haymaker at Mount Alto Hospital, Landry-Gullain-Barré Syndrome.

Lieut. John Schut at Walter Reed General Hospital, Hereditary Ataxias.

Dr. Ira Gore at Mount Alto Hospital Myocarditis.

THE ARMY WINTERED WELL

Throughout the past winter, the Army was in better health than during any like period for which comparable statistics are available. The average January hospital admission rate for the past quarter-century was a little over 14 per thousand troops per week, while the weekly rate for January 1948 was 9.4 per thousand; the February rate was 50 per cent lower than the average for the past twenty-five years. The normal peak load of illness in the Army, as elsewhere, occurs usually in February, due to the increase in respiratory infections. While the present year was no exception, influenza was an almost negligible quantity in the total illness, and other respiratory diseases added comparatively few cases.

OFFICERS REQUEST GRADUATE TRAINING

The following officers have requested graduate training, and their requests were approved at the meeting of the Advisory Board of the Bureau of Medicine and Surgery on March 11: Lieutenants (jg) Walter R. Holland, residency in anesthesia at the Naval Hospital, St. Albans, N.Y.; Neal D. Sanborn, residency in internal medicine at a naval hospital and William R. True, residency in ophthalmology at a naval hospital; Lieutenants Berwyn H. Force, course in internal medicine at the University of Pennsylvania; Robert K. Moxon, residency in internal medicine at the Naval Hospital, Philadelphia; William S. Stryker, residency in children's orthopedics at the Shriners Hospital for Crippled Children, Philadelphia, and David J. McMurray, residency in otolaryngology at the Naval Hospital, Philadelphia; Lieut. Comdr. Bruce M. Shepard, residency in surgery at the Naval Hospital, St. Albans, N.Y.; Comdr. Edward P. Irons, residency in otolaryngology, Naval Hospital, Philadelphia; James W. Gustin, Jr., residency in surgery at Naval Hospital, St. Albans, N.Y.; Joseph J. Timmes, course in surgery at the University of Pennsylvania and Shakeeb Ede, residency in surgery at the Naval Hospital, Long Beach, Calif.

RESERVE MEDICAL DIVISIONS

Naval Reserve volunteer medical divisions have been organized in Charleston, Huntington and Wheeling, West Virginia; the commanding officers are Captains Russel Kessel, William M. Strange and William M. Sheppe, respectively. Other divisions are expected to be organized at Bluefield and Parkersburg. The goal for each medical division includes seventy-five medical officers, fifty nurses, two hundred and fifty hospital corpsmen and fifteen medical service corpsmen.

NUMBER OF CASES OF SCRUB TYPHUS

Preliminary reports indicate that there were 6,850 cases of scrub typhus among Army personnel during World War II and that 280 persons died of the disease; during the same period the Navy reported 613 cases with 28 deaths. The Navy has developed a method for preparing a purified suspension of the causative organism, Rickettsia orientalis, which when used as a vaccine has protected animals against 20,000 times the amount of live organisms sufficient to kill 1 animal. The Navy considers it likely that this discovery will lead to the development of a vaccine that will prevent scrub typhus and also will be useful as a diagnostic aid. Scrub typhus is most prevalent in Japan, Formosa, Malaya and Burma.

AWARDS AND COMMENDATIONS

Dr. Edward A. Strecker

Dr. Edward A. Strecker, professor of psychiatry and head of the department of consultation, University of Pennsylvania, was awarded the Presidential Certificate of Merit at ceremonies held the evening of January 16 at the Naval Hospital, Philadelphia. Dr. Strecker received the award in recognition of his services as consultant to the Surgeon General of the Navy since May 6, 1943.

Commander William J. James

Comdr. William J. James, (MC), U.S.N., chief of the Neurosurgery Department, Naval Medical Center, Bethesda, Md., has been awarded the Bronze Star for meritorious service as medical officer on board the U.S.S. *Randolph* in action against the Japanese forces in the Pacific area from February 16 to July 26, 1945. Dr. James served as senior medical officer and flight surgeon on the *Randolph*. He graduated from St. Louis University School of Medicine in 1937 and entered naval service Aug. 14, 1939.

PUBLIC HEALTH SERVICE

DR. SCHEELE BECOMES SURGEON GENERAL

Dr. Leonard A. Scheele was sworn in as Surgeon General of the Public Health Service at ceremonies held Monday, April 5, in the Federal Security Agency auditorium, Washington, D. C. Dr. L. R. Thompson, a former Assistant Surgeon General, administered the oath of office; also attending were Dr. Thomas Parran, retiring Surgeon General, Oscar Ewing, Administrator of the Federal Security Agency, and representatives of the American Medical Association, medical schools and government agencies.

FULL TIME CANCER DETECTION CENTER

One of the first full time cancer detection centers in the United States is being operated by the cancer control branch of the National Cancer Institute, Public Health Service, as a demonstration unit at Hot Springs, Ark. The center is located in buildings of the Public Health Service rapid treatment center for venereal disease, whose patients it examines exclusively. The staff includes Dr. Byron E. Watts, chief, and other Public Health Service personnel: two physicians trained in cancer diagnosis at Memorial Hospital, New York; two medical officers trained in cytologic technic under Dr. George N. Papanicolaou, and a nurse officer who arranges for the follow-up of patients with lesions. The project is under the supervision of Dr. Allan Koplin, chief, Field Operation Unit, Cancer Control Branch. Specially trained clerical workers take a routine screening history, which is then amplified by the physician. By March 1, 800 patients, all women, had been given complete physical examinations and the cytologic test for cancer. Thus far 8 cases have been discovered. Examination of male patients will be started later.

CANCER RESEARCH FACILITIES

The National Advisory Cancer Council at a meeting in Washington, D. C., March 12 named twenty-one universities and hospitals as being in great need of more facilities to carry on desired scientific projects in cancer research. The council recommended that the $2,053,000 available in funds of the National Cancer Institute for the construction of nonfederal research facilities be stretched as far as possible and where most needed among the institutions named. More than $8,000,000 was involved in the requests favorably considered by the council. The two largest requests for construction grants that were recommended were $1,000,000 each to the University of California Medical School, Berkeley, and College of Physicians and Surgeons, New York, for construction and equipment for the Cancer Research Institute and the Cancer Research Laboratory, respectively.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARIZONA

State Medical Meeting. – The Arizona State Medical Association will hold its annual meeting May 19-21 at the Westward Ho Hotel, Phœnix. The guest speakers will be:

J. Dewey Bisgard, Omaha, Cancer-Ulcer Problem of the Stomach.

Jerome W. Conn, Ann Arbor, Mich., Management of Diabetic Coma.

Irvin E. Hendryson, Denver, Early Diagnosis of Poliomyelitis.

The Woman's Auxiliary will meet at this time.

CALIFORNIA

Typhoid Carrier in High School Cafeteria.--Twenty-one cases of typhoid fever, type C, occurred in high school students in Ukiah, Mendocino County, during January. Epidemiologic investigations by the California Department of Public Health have disclosed that the chief cook in the school cafeteria was a typhoid carrier. Control measures taken at the time of the outbreak included (1) pasteurization of the community's milk supply, (2) closing of the school cafeteria and (3) immunization of the entire high school student body.

Report of Eye Bank.—The Stanford Eye Bank reported March 12 that it had provided thirty-three corneas for eye graft operations during its first year of operation. All qualified eye surgeons on the Pacific Coast have been invited to make use of the facilities of the bank. Corneas collected and preserved by the eye bank are distributed without cost to either patient or surgeon, except for a small service fee for cost of handling the tissue. Information on the correct procedure for registration of donors can be secured by writing to the Stanford Eye Bank, 2398 Sacramento Street, San Francisco.

CONNECTICUT

Doctors Aid Vienna Patients.--An anonymous group of Greenwich physicians is aiding patients in a Vienna, Austria, hospital by providing, through the Greenwich Committee for Foreign Relief, drugs and instruments for the use of fellow professional men in the Austrian capital. Mrs. Samuel K. Meek, committee chairman, recently announced that a shipment prepared by the physicians themselves and sent through the committee has already arrived in Vienna, where a grateful official is utilizing most of it for the care of infants and children.

Yale to Sponsor Graduate Education.—The expansion of Yale facilities for graduate education for Connecticut physicians has been announced, and the appointment of Dr. William R. Willard, New Haven, assistant professor of public health, as associate dean in charge of graduate medical education. Dr. Willard graduated from Yale University School of Medicine, New Haven, in 1934 and received a doctor of public health degree in 1937. He has been deputy state health officer for Maryland and a surgeon of the U.S. Public Health Service. The Connecticut State Medical Society is cooperating in the establishment of the deanship. The expanded program has two aims; (1) provision for short and long refresher courses for Connecticut physicians, and (2) assistance to small Connecticut hospitals in training resident physicians who are preparing to become specialists

DISTRICT OF COLUMBIA

Personal.--Dr. W. Montague Cobb, associate professor of anatomy, Howard University College of Medicine, has been appointed head of the department of anatomy. He is a graduate of Howard University, 1929.

University Opens New Hospital. – George Washington University took possession of its new four hundred bed hospital March 19. The hospital occupies a city square, contains one hundred and twenty single and one hundred and eight double rooms, eighteen wards and forty beds for resident physicians and interns, six air-conditioned major operating rooms, and three smaller ones, nine air-conditioned delivery rooms, nurseries, noise abatement devices, and motion picture equipment to record operating room technics. A large amount of space will be devoted to laboratories and research units. Built at a cost of about $3,897,000, of which $2,820,000 was for construction and fixed equipment and about $850,000 for site acquisition, the outlay per patient bed, estimated on basic cost, was about $9,370. The university, which will staff the hospital, is providing movable equipment and furnishings to cost about $970,000.

ILLINOIS

Chest Physicians Meeting.—The annual meeting of the Illinois Chapter of the American College of Chest Physicians will be held at the Palmer House, Chicago, May 10. The guest speaker will be Dr. Roy A. Wolford, Veterans Administration, Washington, D. C., " The Program of the Veterans Administration on Diseases of the Chest. "

Chicago

Dr. Fulton to Lecture. – The fifth annual D. J. Davis Lecture on Medical History will be given by Dr. John F. Fulton, Yale University School of Medicine, New Haven, Conn., on April 28 in room 221 of the University of Illinois College of Medicine. His subject is " The Position of William Withering in the History of Scientific Medicine.

Annual Zeit Memorial Lecture.—The fifth annual Robert Frederick Zeit Memorial Lecture, sponsored by the Chi Chapter of Alpha Kappa Kappa, will be delivered by Dr. Irvine McQuarrie, professor of pediatrics, University of Minnesota, Minneapolis, in Thorne Hall at Northwestern University, Lake Shore Drive, April 22 at 4 p.m. Dr. McQuarrie, who recently made an extensive trip through the Orient, will speak on " Medical Problems and Practice in Japan. "

Society of Internal Medicine.—The April meeting of the Chicago Society of Internal Medicine will be held April 26 at the Drake Hotel at 8 p.m. A panel on "Massive Albumin Therapy in Disease of the Liver " will be presented by Dr. Robert M. Kark, Chicago, and the invited speakers, Drs. George J. Gabuzda, Chicago, Gordon R. Morey, Westchester, Ill., Robert E. Johnson, Tinley Park, Ill., and Mr. Frank C. Consolazio, Chicago. John S. Gray, Ph.D., Chicago, has been invited to speak on "The Physiology of Dyspnea. "

University Given Bassoe Portrait.—A portrait of the late Dr. Peter Bassoe was presented to the University of Illinois College of Medicine March 26 by the Central Neuropsychiatric Association. The portrait, painted by Oskar Gross, will be hung in the Quine Medical Library. Dr. Bassoe, who died Nov. 5, 1945, was the founder and first president of the Central Neuropsychiatric Association and was a member of a committee appointed by the late Governor Horner to draw plans for the establishment of the Illinois Neuropsychiatric Institute.

KENTUCKY

Society News.--The Jefferson County Medical Society on April 19 will hear Dr. Willard R. Cooke, professor of gynecology and obstetrics at the University of Texas Medical Branch, Galveston, Texas, on "Rationalism in Regard to Gynecologic Operations." He will speak at a dinner meeting at the Pendennis Club at 7 p.m. under the sponsorship of the Louisville Obstetrical and Gynecological Society

LOUISIANA

Alumni Organize.--At a meeting of the Louisiana State University School of Medicine, New Orleans, on March 18, the New Orleans District of the Medical Alumni Association was organized. About seventy-five of over three hundred and fifty alumni practicing in New Orleans were present to hear Dean Vernon Lippard discuss plans for expansion of the school. Officers elected were Dr. Jack R. Anderson, president, and Dr. Philip L. Cenac, secretary-treasurer. Meetings of the association are to be held quarterly.

Graduate Course in Basic Sciences. -- A graduate course in the basic sciences as applied to orthopedic surgery has been established at Tulane University of Louisiana School of Medicine, New Orleans. The course has been made available for the first time to physicians other than those associated with the orthopedic clinics at Charity Hospital, the Veterans' Hospital, Touro Infirmary and Tulane. Divided into four categories, physiology, pathology, bacteriology and anatomy, the course involves twenty-five weeks of instruction. Dr. Jack K. Wickstrom, instructor in orthopedics, is in charge of the course.

MASSACHUSETTS

Appoint Professor of Anatomy.--Dr. Arthur M. Lassek, head of the department of anatomy at the Medical College of the State of South Carolina, Charleston, since 1932, has been appointed Waterhouse professor of anatomy at the Boston University School of Medicine effective July 1, succeeding Dr. Jesse L. Conel, a member of the faculty of the university's school of medicine since 1923. Dr. Lassek previously taught at the University of Washington, Seattle; Northwestern University Medical School, Chicago, and the University of South Dakota School of Medical Sciences, Vermillion. Dr. Conel is retiring to continue his research on the development of the cerebral cortex at different ages of childhood. He plans to publish two more volumes on this subject and is working now on the child at the age of 14 months.

Multiple Sclerosis Clinics.--The first research clinic in a projected series to investigate multiple sclerosis was opened March 29 at the Beth Israel and Boston State hospitals, Boston, through a grant from the National Multiple Sclerosis Society. The Boston clinic will do research on the cause of the disease. Another clinic will be opened in the Albany Hospital, Albany, N. Y., where neurologists of Albany Medical College will cooperate with the New York State Department of Health in conducting the research. As soon as funds permit, the society will establish multiple sclerosis research clinics in leading cities across the country. The project of research clinics has been approved by the society's medical advisory board, of which Dr. Tracy J. Putnam, chief and attending surgeon, department of neurosurgery, Cedars of Lebanon Hospital, Los Angeles, is chairman, and Dr. Thomas M. Rivers, director of Hospital of the Rockefeller Institute for Medical Research, is vice chairman.

MISSOURI

The Seelig Fund.--Friends and colleagues of Dr. Major G. Seelig, St. Louis, have contributed funds to establish an annual lecturship in his honor at Washington University School of Medicine, St. Louis Dr. Seelig retired from the staffs of Washington University Medical School and Barnard Free Skin and Cancer Hospital in January. For twenty-seven years he has been a member of the faculty at the medical school, and for the past seventeen years he had been conducting cancer research. Dr. and Mrs. Seelig are living now at 54 Belleau Avenue. Atherton, Calif.

NEW JERSEY

Society News.--The New Jersey Proctologic Society recently elected Dr. Frank S. Forte, Newark, as president, and Dr. Urban R. Finnerty, Montclair, as secretary.

Organize Allergy Society.--Thirty-three charter members, representing all parts of the state, attended the organizational meeting of the New Jersey Allergy Society February 18 at the Academy of Medicine in Newark. Dr. Nathan Schaffer, East Orange, was elected president; Dr. William C. Greifinger, 31 Lincoln Park, Newark, secretary; and Dr. Frank L. Rosen, Newark, treasurer. Membership is open to physicians interested in the practice of allergy who are members of their county societies. The program of the first scientific meeting at the Academy of Medicine in Newark, May 12, will consist of a panel discussion of hay fever.

NEW YORK

Report of Committee on Cerebral Palsy.--The Joint Legislative Committee to Study the Problem of Cerebral Palsy has presented a report to the Legislature outlining a program to provide medical care, rehabilitation and special education for victims of the disease. The report recommended the establishment of seven centers for diagnosis and evaluation, three within New York City; revision of the formula for state aid to local school districts as it pertains to special education for the physically handicapped; the construction of a state hospital home for those too severely handicapped to live at home; an increase in the number of such cases to be cared for at the New York State Reconstruction Home at West Haverstraw; the development of an enlarged training center and a practice school for teachers of handicapped children at Buffalo State Teachers College; increased training of medical and other personnel needed for the full care of such children, and the immediate development of a plan to discover the names of all children in the state who suffer from orthopedic handicaps. Assemblyman Abraham Schulman Rochester, chairman of the committee, reported that the number of known cases of cerebral palsy among children in the state is 6,000.

Dr. Claude H. Barlow Awarded Certificate of Merit.--The President of the United States has awarded the Certificate of Merit to Dr. Claude H. Barlow, formerly of Trumansburg, for outstanding fidelity and meritorious conduct in aid of the war effort against the common enemies of the United States and its allies. Dr. Barlow went to Egypt in 1929 at the request of the Rockefeller Foundation to conduct research on bilharziasis. He also found that snails common to Egyptian canals and ponds are host to the Bilharzia (Schistosoma) parasite. During the recent war he infected himself with the organism in an effort to find a cure for the disease.

New York City

Personal.--At the January meeting of the Pan-American Ophthalomological Association in Havana Cuba, Dr. Arthur A. Knapp read a paper on "Treatment of Blinding Diseases of the World."

Residencies Available.--The new psychiatric division of the Kings County Hospital, Brooklyn, has a number of residents' positions available for appointment together with opportunities available for degrees in graduate work. The hospital is affiliated with Long Island College of Medicine. The standard resident's salary is $1,560 with maintenance. For information address the director of psychiatry, Dr. Sam Parker, Kings County Hospital, Albany Avenue and Winthrop Street.

Appointments and Promotions.--The following appointments to the faculty of New York University College of Medicine have recently been made: Thomas N. Graham, New York, assistant clinical professor in the department of dermatology and syphilology; Edgar Lawrence and Harry F. Wechsler, New York, assistant clinical professors in the department of medicine; Isidor C. Rubin, Hempstead, N. Y., clinical professor in the department of obstetrics and gynecology; Alfred J. Vignec, New York, clinical professor, department of pediatrics; Allan L. Grafflin, Boston, research associate, department of pharmacology; L. Corsa Reid, New York, associate professor, department of physiology, and William Watson, New York, associate professor, department of physiology. In the postgraduate division appointees from New York include Ira I. Kaplan, clinical professor, and Rieva Rosh, assistant clinical professor of radiology; Bela Mittelman, assistant clinical professor of psychiatry; Sidney Rubenfeld, associate clinical professor of radiology, and Charles R. Rein, associate clinical professor of dermatology and syphilology.

Promotions were as follows: Israel S. Freiman to assistant clinical professor, department of neurology; William M. Dick, associate clinical professor, and Miles Atkinson, assistant clinical professor, department of otorhinolaryngology; Charles Gottlieb, professor of radiology and chairman of the department; William P. Anslow Jr. and Laurence G. Wesson, assistant professors, department of physiology; George G. Deaver, professor of clinical rehabilitation, department of rehabilitation and physical medicine.

Manager of Toxicology Department.--Dr. Arthur G. Cranch retired January 1 as manager of the industrial toxicology department of Union Carbide & Carbon Corporation after twenty-eight years' service with the organization and is being retained as a medical consultant on a part time basis. Dr. Thomas W. Nale, New York, assistant manager of the department for two years, succeeds Dr. Cranch.

Society News.--The Brooklyn Urological Society has recently elected Dr. Frank C. Hamm, Brooklyn, president, and Dr. Harold B. Hermann, Brooklyn, secretary-treasurer.

OHIO

Seminar in Dermatology.--The Society of General Physicians of Cincinnati in collaboration with the Department of Dermatology, University of Cincinnati, will offer a seminar on the treatment of skin disease May 4-27, consisting of sixteen hours of lectures, demonstrations and case presentations. Thirteen members of the department will present the course. Lectures will be so given at the Cincinnati General Hospital that patients may be brought from the dermatology wards to the classroom.

TEXAS

Fund for Cancer Research.—The Damon Runyon Cancer Research Fund and the Variety Club Foundation of Texas recently gave jointly $100,000 to Southwestern Medical Foundation.

Dr. Williams Honored.—Dr. J. Rice Williams, Houston, was guest of honor at a meeting of associates and friends in Houston January 18. A service pin was presented to him in recognition of his fifty-four years as a member of the medical profession; in addition, he was cited for his work in civic affairs. Dr. Williams graduated from the University of Tennessee College of Medicine, Memphis, in 1894 and has practiced in Houston since 1904; since 1938 he has been speaker of the house of delegates of the state medical association.

Appoint Director of Cancer Hospital.—Dr. Charles L. Spurr, formerly on the faculty of the University of Chicago, has been appointed internist and director of the M. D. Anderson Hospital for Cancer Research, Houston. He was graduated from the University of Rochester School of Medicine and Dentistry in 1940 and was instructor at the University of Chicago for four years before serving in the U. S. Navy.

Dr. Gilbert H. Fletcher, who made a tour of European hospitals to observe methods of radiation therapy, has been appointed radiotherapist at the hospital. He was graduated from the University of Brussels in 1941, was an instructor at Cornell University Medical College, New York, from 1941 to 1945 and was radiologist in the United States Army from 1945 to 1947.

WEST VIRGINIA

State Medical Association Meeting.--The annual convention of the West Virginia State Medical Associatiin will be held at the Hotel Prichard, Huntington, May 10-12. An innovation will be round table breakfasts at which matters of general interest will be discussed. Guest speakers will be:

MONDAY

J. Warrick Thomas, Richmond, Va., Cutaneous Allergies.
Henry M. Goodyear, Cincinnati, Use of Chemotherapy and Antibioticsin the Treatment of Upper Respiratory Infections.
John B. Barnwell, Washington, D.C., Streptomycin and Tuberculosis.
Jean S. Felton, Oak Ridge, Tenn., Industrial Medicine.
Sophia J. Kleegman, New York, Diagnosis and Treatment of Infertility in Women.

TUESDAY

Perrin H. Long, Baltimore, Treatment of Infectious Hepatitis.
Emil Novak, Baltimore, Management of the Menopause.
Francis F. Schwentker, Baltimore, Pneumonia in Children.
J. Edwin Wood, Charlottesville, Va., Use of Low Sodium Diets in Treatment of Hypertension.
Russell L. Haden, Cleveland, Gout.
George F. Lull, Chicago, Secretary and General Manager, American Medical Association, Trends in Medical Service.

WEDNESDAY

Austin I. Dodson, Richmond, Va., Recent Advances in Urology.
Miller Francis Turney, Brooklyn, Cervical Disks.
Fred S. Rankin, Lexington, Ky., Surgical Treatment of Cancer of the Lower Gastrointestinal Tract.
J. Steward Rodman, Philadelphia, Carcinoma of the Breast.

The annual meeting of the Woman's Auxiliary will be held at the Frederick Hotel.

GENERAL

Hearing Society Changes Address.--The American Hearing Society, which has been housed for twenty-five years in the Volta Bureau Building, 1537 Thirty-Fifth Street N.W., on April 1 moved to 817 Fourteenth Street N.W., Washington, D.C.

Society News.—At the annual session of the American Academy of Pediatrics, Dallas, Texas, in December, Dr. John A. Toomey, Cleveland, was installed as president. Dr. Clifford G. Grulee, Evanston, Ill., continues as secretary.

Pharmaceutical Convention in Cuba. — The convention of the American Pharmaceutical Manufacturer's Association met April 12-14 at the Hotel Nacional de Cuba, Havana. The association's research award was presented to Dilworth Wayne Woolley, Ph.D., of the Rockefeller Institute, for his scientific achievements in nutrition. Dr. Roscoe L. Sensenich, South Bend, Ind. President-Elect of the American Medical Association, and Dr. Austin Smith, Chicago, Secretary of the Council on Pharmacy and Chemistry, discussed basic research of drug therapy.

Meeting of American Hearing Society.--The National Conference of the American Hearing Society will be held at the William Penn Hotel, Pittsburgh, May 19-22 under the presidency of Dr. C. Stewart Nash. Physicians speaking at the conference include:

Dean M. Lierle, Iowa City, Recent Advances in the Medical Treatment of Deafness.

Morris Fishbein, Editor, THE JOURNAL, Chicago, Is It Worth Hearing?

Emily A. Pratt, Washington State Department of Health, Prevention and Conservation of Hearing.

Among other subjects to be discussed are goals of group activities in hearing societies, hearing aid advisory centers, aural rehabilitation of adults and educational program for children with a hearing loss.

International Congress on Obstetrics and Gynecology.—The American Committee on Maternal Welfare in conjunction with the fourth American Congress will sponsor an International Congress on Obstetrics and Gynecology at the Hotel Pennsylvania, New York, May 14-19, 1950. Preliminary plans include a program in which each morning will be devoted to formal presentation and discussion of a general topic and each afternoon will be given over to round table and informal discussion of the subjects. Clinics will be developed in the medical centers of the country so that foreign visitors may acquaint themselves with the advances of American institutions. Inquiries should be addressed to the general chairman, Dr. Fred L. Adair, 24 West Ohio Street, Chicago 10.

Student Health Association. -- The American Student Health Association will hold its annual meeting May 6-8 at the Hotel Statler, Detroit, under the presidency of Dr. Harry D. Lees, Philadelphia. Among the speakers will be:

Joseph A. Johnston, Detroit, Metabolism of Adolescence.

Robert B. Clarke, Ann Arbor, Mich., Neurologic Problems of College Students.

Donald M. Pillsbury, Philadelphia, Management of Acute Eruptions of the Skin.

E. Lee Shrader, St. Louis, and William G. Beadenkopf, Chicago, Influenza Vaccine.

Chris J. D. Zarafonetis, Ann Arbor, Mich., Infectious Mononucleosis.

A panel discussion of "The Changing Problems of Administration in Student Health Services" will conclude the program.

Life Insurance Medical Research Fund.--Thirty-one hospitals, medical colleges and research clinics in eighteen states and Canada will share $484,790 in grants from the Life Insurance Medical Research Fund during 1948 for research in heart disease. In addition, fourteen individual physicians will receive $52,600 in fellowships, two of them for work outside their country. Fellowship stipends vary from $2,500 to $4,000. The awards bring the total sum made available for aid to medical research by the Life Insurance Medical Research Fund since its organization in December 1945 to approximately $1,800,000. The fund is supported by one hundred and forty-nine life insurance companies in the United States and Canada and is administered through a board of directors representing the life insurance business and an advisory council of medical research experts. Dr. Francis B. Dieuaide, clinical professor of medicine, Columbia University College of Physicians and Surgeons, is the scientific director.

Courses for Medical Record Librarians.—A second workshop for registered record librarians is to be held in Denver May 24-28 at the Cosmopolitan Hotel. This will be presented by the Extension Course Division of the American Association of Medical Record Librarians with the cooperation of the University of Colorado Medical Center and the Colorado Association of Medical Record Librarians. A regular one week extension course will be given at St. Louis University, St. Louis, from June 14-18. This course is designed to present fundamentals for proper understanding of record work and to assist those who are of necessity working with the Standard Nomenclature of Disease without having received training in its use. Enrolment is open to all persons working in the medical record department of a hospital. Further information about either of these courses may be obtained from Mrs. Edna Huffman, Field Representative, Extension Course Division, American Association of Medical Record Librarians, 22 East Division Street, Chicago 10.

Drs. Taussig and Blalock to Receive Award.--The 1948 Passano Foundation award will be presented to the Taussig-Blalock team which developed the operation popularly known as the "blue baby operation". Presentation of the $5,000 cash award will be made June 23 at the Palmer House, Chicago, during the Annual Session of the American Medical Association. Dr. Helen B. Taussig is associate professor of pediatrics and Dr. Alfred Blalock is professor of surgery at Johns Hopkins University School of Medicine, Baltimore. Since this operation was first undertaken in November 1944 more than 600 patients drawn from all parts of the world have been operated on at Johns Hopkins Hospital alone.

The Williams & Wilkins Company of Baltimore established the Passano Foundation in 1944 to aid in the advancement of medical research, especially research which promises clinical application.

Marriages

MARTIN S. KLECKNER Jr., Allentown, Pa., to Miss Barbara A. Luse of Oil City, February 7.

DAVID LATHAM TABER, Rockville Centre, N. Y., to Miss Jean Dennison of Gloversville, Dec. 17, 1947.

CLARENCE E. PHILLIPS, Sunbury, Pa., to Miss Jean R. Kiger, of Northumberland, at Williamsport, Md., Dec. 28, 1947.

DAVID J. ROSE to Miss Edith R. Sprung, both of New York, February 15.

Deaths

Midian Othello Bousfield ⊕ Chicago; born in Tipton, Mo., Aug. 22, 1885; Northwestern University Medical School, Chicago, 1909; past president and since 1934 chairman of the commission on hospitals and medical education of the National Medical Association; fellow of the American Public Health Association and of the Institute of Medicine of Chicago; first Negro member of the board of education and former director for Negro health of the Rosenwald Fund; served as consultant to the U.S. Children's Bureau and the Chicago Board of Health; a member of advisory committees to various national, state and local government agencies; formerly a member of the planning committee, White House Conference on Children; in the field of social work served the Chicago and the National Urban League and the Y.M.C.A.; vice president and medical director of the Supreme Liberty Life Insurance Company; member of the board of trustees of Provident Hospital; during World War II organized Station Hospital 1 at Fort Huachuca, Ariz., of which he became a commanding officer; for his services received the Legion of Merit; retired Nov. 9, 1945 with the rank of colonel; died February 16, aged 62, of angina pectoris.

Thomas Dwight Sloan, Charlottesville, Va.; born in Ripley, Tenn., Dec. 6, 1879; University of Virginia Department of Medicine, Charlottesville, 1909; instructor in chemistry at the University of Virginia from 1905 to 1909; engaged in medical missionary work in Nanking, China, where he served as professor of clinical medicine at the University of Nanking and superintendent of the University Hospital; medical superintendent of the Peking Union Medical College Hospital from 1922 to 1925; in 1925 became assistant director in charge of the Lakeside Hospital in Cleveland and later superintendent of the New York Post-Graduate Medical School and Hospital in New York; formerly medical superintendent of the Flagler Hospital in St. Augustine, Fla.; died January 10, aged 68.

Franklin Ramsdell Hughes ⊕ Cape May, N.J.; born in 1879; Hahnemann Medical College of Philadelphia, 1906; past president of the Cape May County Medical Society; during World War I served on the county advisory board; an examining physician on a local board of the selective service during World War II; formerly county coroner; medical examiner for the schools of Cape May; associated with the boards of health of the lower township West Cape May and Cape May for many years; medical officer in charge of the U.S. Public Health Service Relief Station from 1926 to 1945; on March 25, 1945 awarded an honorary degree of Doctor of Science by his alma mater; died in the Hahnemann Hospital, Philadelphia, February 5, aged 68, of aneurysm of the aorta.

Edwin Hulme McIlvain, Philadelphia; born in Millville, N.J., in 1887; Temple University, School of Medicine, Philadelphia, 1912; member of the American Medical Association; since 1915 medical director of the Budd Company; for many years lecturer on medical jurisprudence at his alma mater; a director of the Philadelphia Health and Tuberculosis Association; a vice president of the Tioga National Bank; a member of the city chamber of commerce; died January 15, aged 60, of hypertensive cardiovascular renal disease.

John E. Womack ⊕ Staunton, Va.; Medical College of Virginia, Richmond, 1909; served as secretary treasurer of the Augusta County Medical Society; during World War I a captain in the medical corps of the U. S. Army and during World War II chairman of the medical examining board of the local selective service board; at one time city health officer; affiliated with the King's Daughters' Hospital, where he died January 7, aged 65, of cerebral hemorrhage, arteriosclerosis and hypertension.

Robert Herbert Wright, Newton Center, Mass.; University of Virginia Department of Medicine, Charlottesville, 1900; member of the American Medical Association and of the Medical Society of Virginia; formerly associate professor of ophthalmology at the Medical College of Virginia in Richmond; fellow of the American College of Surgeons; formerly on the staff of the Stuart Circle Hospital in Richmond; died Dec. 22, 1947, aged 68, of coronary thrombosis

Thomas Bayson Aycock ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1924; professor of clinical surgery at his alma mater; member of the American Association for Thoracic Surgery and of the Southern Surgical Association; member of the founders group of the American Board of Surgery; affiliated with the Baltimore City Hospitals, Bon Secours Hospital and the University Hospital; died January 7, aged 52, of cerebral hemorrhage.

Linus Terrell Baker ⊕ Dixie, La.; University of Nashville (Tenn.) Medical Department, 1908; served on the staff of Highland Sanitarium in Shreveport; awarded the Silver Beaver posthumously by Norwela Council of Boy Scouts of America for outstanding service to boyhood; died suddenly January 26, aged 62, of heart disease.

William Hulbert Banks ⊕ Yakima, Wash.; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1900; served on the staff of St. Elizabeth's Hospital; died Dec. 24, 1947, aged 73.

Louis Henry Behrens ⊕ St. Louis; Missouri Medical College, St. Louis, 1894; past president of the St. Louis Medical Society; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine; affiliated with the Barnes, Deaconess, Jewish and DePaul hospitals; director of the Municipal Opera; died January 1, aged 79, of myocardial infarction.

Freeman Elisha Bennett, Belfast, Maine; Medical School of Maine, Portland, 1899; formerly a member of the state legislature; died Nov. 29, 1947, aged 77, of pulmonary edema and Parkinson's disease.

Charles Frank Boucek, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1896; member of the staff of St. John's General Hospital; director of the Provident Trust Company; president of the Dixon Motor Company; died January 17, aged 72, of osteosarcoma.

Edward Sinnet Bowman, Davenport, Iowa; State University of Iowa College of Medicine, Iowa City, 1893; died January 4, aged 79.

Mary Alice Brosius, Washington, D. C.; Columbian University Medical Department, Washington, 1894; Southern Homeopathic Medical College, Baltimore, 1895; on the courtesy staff of the Homeopathic Hospital; died January 20, aged 89, of gastrointestinal hemorrhage.

Foreign Letters

LONDON

(From Our Regular Correspondent)

April 2, 1948.

Annual Meeting of British Medical Association

The next annual meeting of the British Medical Association will be held at Cambridge from June 25 to July 2 under the presidency of Sir Lionel Whitby, regius professor of physic in the university. The scientific work will be divided into nineteen sections, which will meet on the three days, June 30 - July 2. The sections, with their presidents, are as follows: medicine, Dr. L.B. Cole; surgery, Mr. Vernon Penn Pennell; obstetrics and gynecology, Mr. J.R. Campbell Canney; anethetics, Dr. Z. Mennell; child health, Sir Leonard Parsons; diseases of the chest, Dr. R.R. Traill; occupational health, Dr. Donald Stewart; ophthalmology, Mr. O. Gayer Morgan; orthopedics, Professor T.P. McMurray; pathology and bacteriology, Professor H.R. Dean; physiology including biochemistry, Professor A.C. Chibnall, F.R.S.; preventive medicine, Dr. G.F. Buchan; radiology, Dr. S.C. Shanks; anatomy and anthropology, Professor H.A. Harris; dermatology, Dr. C.H. Whittle; neurology and psychiatry, Professor E.D. Adrian; nutrition, Professor R.A. McCance; otorhinolaryngology, Mr. V. E. Negus, and pharmacology, Professor E. B. Verney, F.R.S.

The following are among the subjects chosen for discussion: thiouracil in the treatment of thyrotoxicosis ; the modern management of macrocytic anemias; surgery in hypertension; tuberculous adenitis; cancer of the breast; the problem of infertility and its treatment; analgesia in midwifery; management of the third stage of labor and its complications; anesthesia for thoracic surgery; neonatal mortality; malignant disease in infancy and childhood; bronchial carcinoma; relation between upper respiratory infection and radiologic infection and radiologic appearances of the lungs; surgery of congenital heart disease; the present treatment of pneumonia; human relations in industry; aviation medicine; ophthalmic problems associated with gynecologic and obstetric conditions; the significance and interpretation of refraction; contact lenses; the heredity of eye diseases; nutritional eye diseases; clinical significance and treatment of lesions of the intervertebral disk; the operative treatment of fractures; injection treatment of osteoarthritis; advances in our knowledge of the Rhesus factor; acute and subacute hepatitis; recent work on proteins and its medical applications; plasma and blood derivatives in the treatment of burns; occupational dermatitis; investigation and treatment of epilepsy of late onset; early recognition and management of senile degeneration, affections of the sphenoid sinus and their treatment; antihistaminic substances, and agents determining and influencing the functions of the pars nervosa of the pituitary.

New Health Regulations for Air Travel

New measures to reduce the risk of aircraft or travellers by air bringing into this country disease from abroad have come into force on April 1. The speed of air travel has produced special medical problems. For instance, while a journey from India to London by sea normally takes three weeks, during which any infectious illness on board would become known and could be dealt with at the port of arrival, a passenger by air can fly from Singapore in two days and from India or South Africa in thirty-six hours. This time is much shorter than the normal incubation period of plague, cholera, yellow fever, typhus and smallpox — the diseases with which international control is mainly concerned.

An International Sanitary Convention on air travel was drawn up in 1933 and extended in 1944 to standardize the measures which may be taken for the control of infectious diseases when an aircraft passes from one territory to another. The first public health regulations for aircraft in this country came into force in 1938; with the nationalization of airfields and the changing conditions of air travel, they have now been replaced by new regulations. All incoming aircraft from places abroad will be met by medical officers. On arrival the commander of the aircraft will give the names of the places in which it has been during the last fourteen days. Passengers showing no symptoms of an infectious disease will be given a card setting out the simple precautions to observe if they fall ill within twenty-one days of arrival. These include showing the card to their physician, who thus learns that his patient has recently arrived from abroad, where he may have been exposed to infection. If there is any doubt about the nature of the illness, the physician is to inform the health officer of the area at once. Thus all cases of illness in travellers arriving by air from abroad can be traced and the health authorities can take the necessary precautions, including isolation of the sick and the supervision of contacts. The regulations also apply to aircraft which, because of emergency or other reason, alight outside a customs airport.

Dentists Reject Work Under Health Service Act

The representative board of the British Dental Association has adopted a resolution recommending that dentists refuse to enter service under the National Health Service Act until it is so amended as to include the principles advocated by the association. The resolution, which was adopted by 85 votes to 4, recorded that the board considered the proposals to be not in accord with the principles essential for a satisfactory dental service for the nation. The provisions of the act would curtail the dentist's clinical freedom to the detriment of the standard of treatment. The method of remuneration on which the Minister insists, payment of a fixed sum for each item of treatment, irrespective of any special skill employed or the amount of time involved, would put a premium on hurried and shoddy work.

Suffocation Of Infants By Milk Feeds

From time to time cases are reported from the coroners' courts of infants suffocated by inhalation of vomited milk feeds. This accident is particularly liable to occur in weakly infants, those mentally defective and those suffering from malformations such as cleft palate. In consequence of an editorial on the subject published in the Lancet, C.J. Polson and D.E. Price, of the department of forensic medicine of the University of Leeds, have published (*Lancet* 1:343 Feb 28. 1948) an analysis of recent cases coming under the jurisdiction of

the Leeds coroner's court. In the years 1945–1947, 21 infants aged 9 months or less died of inhalation of vomit. The annual incidence in these three years was 6 per cent, 9 per cent and 15 per cent, respectively, of all deaths of infants, excluding stillbirths, examined in the city mortuary in these years. The depositions suggested that the same cause was responsible for the deaths of at least another 10 infants, in whom the cause of asphyxia was not ascertained or was reported to be some other factor such as convulsions. Soft feather pillows were held to be responsible for 2 deaths and probably responsible for another 4. In 1 case a shawl was believed responsible for preventing the free escape of vomit and so predisposing to its inhalation. Some of the infants were described as "windy," or prone to retch or vomit after feeds, while lying down, and it was a common practice to allow infants to suckle at the bottle when laid in their perambulators or cots. The stomach contents, several hours after the last feed, were distinctly in excess of what was ordinarily to be expected. The kind of food was recorded in 16 cases. Of these, 9 had national dried milk, 4 had "ostermilk," while 3 (of which 1 had a supplementary feed of cows' milk and water) were breast fed. One observer, Gardner, has recorded a predominance of artificially fed infants among his cases. The lesson drawn from these cases is that the preparation of artificial milk foods must be carefully performed if lumps are to be avoided. Lumps in the feed may be ingested by the infant if the nipple on the bottle is worn or its opening deliberately enlarged. But there is no information that the ingestion of lumps is in any way injurious or productive of vomiting.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANIERO, March 5, 1948.

Tuberculin and Roentgenologic Observation in BCG Vaccinated Children

Dr. Carlos M. Valente, of the Rio de Janeiro City Health Department, published a report on 1,288 children from 12 months to 16 years of age, subjected to the Mantoux tuberculin test and roentgenographic examination. Of these children, all living in a presumably tuberculous environment, 668 had been orally vaccinated with BCG at birth and 620 had not been immunized. Most of them belonged to the poorest classes of the population. According to the tuberculin tests, a decided prevalence of weak specific hypersensitivity could be disclosed in the immunized children. Among the 620 nonvaccinated children a much higher degree of sensitivity to tuberculin was disclosed. On roentgenographic examination of the 620 children, 1.8 per cent manifested residual tuberculosis, 0.6 per cent were suspected of infection and 1.2 per cent had active forms, 5 of the children with bacteriologic evidence of tubercle bacilli. The author concludes that since a definite protection was evidenced in the BCG-vaccinated children in tuberculous environments it is advisable to expand the practice of BCG immunization as a means of fighting the high incidence of the disease in the city.

Rheumatoid Arthritis and the Heart

The problem of rheumatic and rheumatoid arthritis and its relation to the heart is being studied in Brazil, where rheumatism is not such an important etiologic factor of cardiac diseases as in colder climates. Dr. Oswaldo Lucchesi recently published an analysis of 50 cases. The group included 13 men and 37 women, the former varying between 22 and 66 years of age and the latter between 22 and 65 years of age. The duration of the disease in the whole group varied from one month to forty-one years. The clinical examination showed abnormal heart sounds in 24 patients, but in none of them did the abnormalities present any likeness to the rheumatic type. The radiographic examination disclosed 20 patients with enlargement of the heart due to hypertension. The electrocardiograms were normal in 37 patients, the remaining 13 patients exhibiting abnormalities of nonrheumatic type. Of the 14 patients with rheumatic subcutaneous nodules, 7 showed normal clinical signs, heart size and electrocardiograms. In 7 others Dr. Lucchesi reported the observation of an enlarged left ventricle due to hypertension, causing left axis deviation in 4 cases. He concludes that his observations emphasize the difference between real rheumatic fever and rheumatoid arthritis.

Sickle Cell Disease

Dr. Edgard Boturao, of the Misericordia Hospital of Santos, state of São Paulo, published a report on the hematologic study of 358 patients, including about 20 with sickle cell disease. Of the 358 patients, 64 were white, 132 mulatto and 162 Negro, with the percentage of incidence of sickle cells zero, 4.5 and 8.6, respectively. These results show that the incidence of the disease increases in direct ratio to the intensity of pigment. Dr. Boturao points out the importance of the problem at Misericordia Hospital, where 1,946, or 27.5 per cent, of the 7,078 patients admitted during the last nine months were Negroes.

Thymol Turbidity Test in Experimental Poisoning

Dr. Gilberto G. Villela, of the Oswaldo Cruz Institute, tried to ascertain the value of Maclagan's thymol turbidity test in experimental poisoning with carbon tetrachloride, chloroform, sulfanilamide and "dicumarol." Using the technic recommended by Shank and Hoagland, he performed the tests with the serums of 24 rabbits and 18 rats. The normal values were tested with the serums of 10 rats and 8 rabbits. Since the normal blood of these animals manifested with the thymol reagent only slight turbidity (less than 0.2 unit), larger amounts of the reagent were used (0.2 to 0.4 cc. and 5 cc. Only 20 to 30 per cent of the poisoned animals showed positive reactions (around 2 units). The test was performed with blood collected during and after the poisoning (from two to fourteen days). Notwithstanding, appreciable changes were not observed. For controls, the reaction was tried on 47 normal human serums and on serums from patients with hepatic diseases. Normal serums had turbidity values below 4 units. Dr. Villela concluded that the thymol test is unable to detect hepatic damage produced by drugs like sulfanilamide, chloroform, carbon tetrachloride and "dicumarol." He also suggested that the disturbances in the serum beta-globulin responsible for the positive thymol test appearing in infectious hepatatis and in cirrhosis of the liver are probably not produced by the hepatotoxic agents.

Correspondence

EPILEPTIC PERSONS ARE UNSAFE DRIVERS

To the Editor: --There is a California law which requires that epilepsy, interpreted as " lapses of consciousness which may become chronic," be reported by the attending physician to the state board of health. In this way the epileptic driver is discovered and the use of a license is revoked. A similar law exists in the states of Oregon, Wisconsin and Indiana. The hospital of the University of California has in its files records of many dramatic instances of accidents caused byepileptic persons who have experienced seizures while driving automobiles. It is my impression that if a similar law is enacted in other states, it will mean a substantial contribution toward the prevention of motor vehicle accidents. Dr. W. E. Carter, director of the outpatient department, will provide further information on this subject. Likewise, Mr. Fred Williams, Motor Vehicle Department, Sacramento, Calif. has listed casualties known to have occurred while epileptic persons were driving .

R. WARTENBERG, M.D.
San Francisco, Calif.

RECENT ADVANCES IN TREATMENT OF PULMONARY DISEASE

To the Editor:—In the January 31 issue of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, page 311, the article by James Waring, M.D., on Recent Advances in the Treatment of Pulmonary Disease presents a confusing contradiction of ideas in regard to the therapy of tuberculosis with streptomycin.

In an early paragraph it is stated that "the most experienced men say that they have seen no patient who regretted taking the drug and no patient to whom they regretted giving the drug." Despite this statement, the remainder of the article is filled with warnings against the use of streptomycin. The author also mentions "complete paralysis of both lower extremities with paralysis of bladder and bowels" following intrathecal administration of streptomycin. Dr. Waring further states that some experts "are hopeful that one way or another damage to the vestibular branch of the eighth nerve can be avoided or minimized."

In discussing the future of antibiotic therapy he expresses the hope that a new and safer antibiotic will be discovered. Finally, he states that "the drug is toxic and the immediate and remote bad effects are not accurately predictable", and further mentions that the development of bacterial resistance may leave the patient with an incompletely eradicated infection. I feel that if these are effects of streptomycin therapy there certainly must be both physicians who have regretted giving and patients who have regretted receiving the drug.

RICHARD E. WINTER, M.D.,
New York.

The Letter of Dr. Winter was referred to Dr. Waring, who replies:

The statement about the gratifying experience of "the most experienced men" is correct but my critic fails to appreciate the significance and the emphasis on the phrase "the most experienced men." Perhaps these men were overoptimistic, I am not sure! At any rate, even though experience with streptomycin was admittedly limited and more time was sorely needed for adequate appraisal of its possible good effects as well as its possible bad effects, five things seemed clear as of June 1947: 1. Streptomycin had a remarkable restraining influence on the growth of the tubercle bacillus in culture. 2. It had an astonishingly beneficial influence on tuberculosis in the experimental animal. 3. It had apparently a remarkably beneficial effect on the acute exudative lesions of tuberculosis infection in man. 4. In dosage then prevailing, it frequently damaged the vestibular nerve. 5. After some weeks of its use against human tuberculosis, the organism responsible for the disease frequently showed greatly increased resistance to the antibiotic.

Since June 1947, further experience with streptomycin indicates that a dose of 1 Gm. daily for seven to nine weeks will only rarely cause damage to the vestibular nerve, a confirmation of the hope expressed in my paper. Also, this damage is not serious and is usually well compensated.

We need to know much more about "bacterial resistance." Opinion differs as to its importance, but I am fearful that unless modification of the drug itself or, less likely, modification of dosage schedule can prevent the development of bacterial resistance, the use of streptomycin in human tuberculosis may be greatly limited. This matter of bacterial resistance is disturbing not merely because the organism is no longer inhibited by the drug but for other reasons. If streptomycin is used, sputum converted from positive to negative and a good arrest apparently secured but relapse occurs at the end of one to two years, with a "bacterial resistant" organism now present in the sputum, is cure by nonantibiotic methods now more difficult? In other words, is the patient now worse off than if he had never taken streptomycin? If streptomycin is used with prompt apparent benefit without sputum conversion and without apparent arrest and in a few months a bacterial resistant organism appears in the sputum, is cure by nonantibiotic methods more difficult? Is the patient worse off than if streptomycin had not been used? When bacterial resistance appears, the disease may coincidentally get out of hand! When bacterial resistance appears, is the resistance of the patient to spread of the disease also considerably reduced? We need answers to these questions, which will be answered with time and more experience. Meantime, I reiterate all the warnings in my communication.

I suggest that my correspondent follow the injunctions in my answer to the question " home treatment." In conclusion, let me say that I never wrote anything yet that I could not improve by rewriting.

JAMES WARING, M.D.,
Denver.

Miscellany

TUMOR REGISTRIES

A tumor registry functions as a unit where all cases of certain kinds of tumor may be completely reported, including the history of the patient, roentgenograms of the area involved, stained slides of the tissue examined, a complete report of the diagnosis, and follow-up of the treatment. The first tumor registry was founded by Dr. Emory A. Codman of Boston and embraced the field of bone sarcoma. Dr. Codman soon discovered that conducting a registry was too big a task for one man, so he turned the idea over to the American College of Surgeons, which formally founded a Registry of Bone Sarcoma in 1921. This registry has been in continuous operation at the home of the American College of Surgeons in Chicago ever since, and now more than 3,000 cases of bone sarcoma are registered there. A year after the founding of this registry, the American Academy of Ophthalmology and Otolaryngology contacted the Army Medical Museum, which housed the Army Institute of Pathology, and at their suggestion the Registry of Ophthalmic Pathology was established. This was the first registry instituted by this group, which since then has become known as the American Registry of Pathology, and which now includes a total of fifteen registries. The American Registry of Pathology functions along with the Army Medical Museum as a unit of the Army Institute of Pathology in Washington, D. C.

The other fourteen registries located in the American Registry of Pathology, with the year in which they were established and the sponsor are as follows: the Registry of Otolaryngological Pathology, 1935, American Academy of Ophthalmology and Otolaryngology; the Bladder Tumor Registry, 1927, the Kidney Tumor Registry, 1940, and the Prostatic Tumor Registry, 1943, all sponsored by the American Urological Association; the Lymphatic Tumor Registry, 1925, the American Association of Pathologists and Bacteriologists, the Registry of Dermal Pathology, 1938, the American Academy of Dermatology and Syphilogy; the General Tumor Registry, 1937, the American Society of Clinical Pathologists; the Chest Tumor Registry, 1942, the American Society of Thoracic Surgeons; the Registry of Neuropathology, 1943, the American Association of Neuropathologists; the Registry of Orthopedic Pathology, 1943, the American Academy of Orthopedic Surgeons; the Registry of Gerontology, 1945, the Society for the Study of the Aged; the Registry of Radiologic Pathology, 1947, the American College of Radiology, the American Roentgen Ray Society and the Radiological Society of North America; two special registries, the Registry of Dental and Oral Pathology, 1933, the American Dental Association, and the Registry of Veterinary Pathology, 1944, the American Veterinary Medical Association. The fifteen registries located in the American Registry of Pathology provide an extraordinary accumulation of data on cancer cases, since practically every one of the registries deal with tumor tissue. Pathologic material and related clinical, laboratory, roentgenologic and other data are collected and organized so that the cases can be properly processed and made available for study and research. As living patients are followed periodically, eventually there will be a significant number of life histories of any particular condition to form a basis for definitive studies. The National Research Council, Division of Medical Sciences, has appointed a Committee on the American Registry of Pathology, which serves as an advisor in general administrative, fiscal and professional matters and passes on applications for new registries, submitting recommendations to the Surgeon General of the Army. The Committee is composed of outstanding representatives in the larger specialties. Other registries which are conducted include the Brain Tumor Registry, which is better known as the Cushing Collection at Yale University Medical School, first started by the late Dr. Howard B. Cushing. Dr. Harold Dargeon, director of the Children's Clinic at Memorial Hospital in New York City, has started a Children's Tumor Registry, and records of many unique cancers which affect younger persons are being collected there. The Children's Tumor Registry was formed one year ago for the purpose of collating data with regard to malignant tumors in children and providing a service of consultation. Material will be provided which is based on these two points and is of educational value to professional and lay groups.

Many states are organizing registries for all cases of tumor and cancer. Six states already have well organized units, and these are all part of the diagnostic pattern from which the unique cases reach the national registries. Many state divisions of the American Cancer Society are assisting in the establishment of these registries. The American Cancer Society makes a yearly grant through the National Research Council to the overhead operation of the American Registry of Pathology. The tumor registries are an important link in the overall problem of cancer: early and accurate diagnosis—followed by prompt and adequate treatment (*Cancer News*, January 1948).

Medical Motion Pictures

FILM REVIEW

Know Your Baby. 16 mm., color, sound, 400 feet (one reel), showing time ten minutes. Produced by Crawley Films, Ottawa, in cooperation with the Canadian Committee on Children for the National Film Board of Canada. Procurable on rental or purchase from the National Film Board of Canada, 400 West Madison Street, Chicago 6, and 620 Fifth Avenue, New York 20.

This is a clearly conceived and well constructed film designed to depict the ideal care of a child during the first few months of its life. In logical continuity the film illustrates the proper feeding, bathing and handling of the infant; at the same time it stresses the essential emotional relationship to be cultivated among the child, its mother and its siblings. (Inexplicably, the role of the father is omitted.) Despite minor defects the visual sequences are cogent, interesting and skilfully edited. The vocal commentaries are likewise clear and pertinent. Nevertheless, the film might advantageously be issued in a silent version appropriately subtitled so that it could be more widely shown to expectant parents and others in places where sound projectors are not readily available. The film can be highly recommended for the lay and professional instruction of all who are concerned with psychobiologic welfare of the future adult in his tenderest months of life.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Employee's Refusal to Undergo Spinal Puncture.—The petitioner filed a claim for compensation for a spinal injury received during the course of his employment and, from a judgment in favor of the employer, appealed to the Supreme Court of Tennessee.

The petitioner alleged that he cannot walk in the dark, that he staggers when he does walk, and that he has violent pains in the back and stomach with occasional vomiting. His pupils are contracted "and reacted to light but not to accommodation." Expert testimony was to the effect that these symptoms strongly indicate syphilis in the tertiary stage, at which stage this disease can be verified only by an examination of 3 or 4 cc. spinal fluid. The only way to obtain this specimen is by injecting a needle into the soft tissue and between the vertebrae, the total penetration being usually from 3 to 5 inches (7.62 to 12.7 cm.) A local anesthetic applied to the cutaneous surface eliminates the only possible pain. There is no bleeding and no infection results, but the patient is hospitalized for a few hours after the puncture to prevent headache. This means of procuring a specimen of spinal fluid has been employed by medical science for many years, and there is no record of resulting death, injuries or fainting. If the puncture is performed in an unskilled manner, paralysis lasting to a maximum of four hours may result. The physician proposed by the employer to perform the examination was an expert of recognized standing, and the employer proposed to pay all expenses. The petitioner refused to permit any physician to extract this fluid because he was afraid it might result in death or permanent injury, although he offered no evidence of any possibility of such results other than to say that he once heard that a distant kinsman was injured permanently in this manner.

The Tennessee workmen's compensation law provides that: "The injured employee must submit himself to the examination by the employer's physician at all reasonable times if requested to do so by the employer.... If the injured employee refuses to comply with any reasonable request for examination...his right to compensation shall be suspended and no compensation shall be due and payable while he continues such refusal."

It is generally held, said the supreme court, in construing this law that a reasonably made request by an employer for a surgical operation which is not attended with extraordinary pain or suffering or danger to life or health and which offers appreciable prospect for relief is a reasonable request which the employee must either grant or release the employer from further obligation, at least as long as he refuses. By appropriate analogy, the supreme court continued, and what seems to us to be sound principle, we hold that when it reasonably appears that the affliction of the employee may be due to some cause not arising out of and in the course of employment, then a request for such necessary examination as will determine whether the illness is due to such cause is not unreasonable, if it satisfactorily appears without contradiction that the conducting of such an examination is not attended with appreciable pain or suffering or danger to life or health. In the case at bar, said the court, it reasonably appears that plaintiff in error may be suffering from syphilis in the tertiary stage. The only way known to medical science to certainly determine whether he is suffering from such syphilis is to examine a specimen of his spinal fluid. The obtaining of that specimen requires the doing of an act to his body which is not attended with appreciable pain, suffering or danger to life or health. The examination falls within the same class as that which requires a specimen of blood. The examination requested, the supreme court concluded, is in our opinion entirely reasonable, and the refusal of the employee to submit thereto is arbitrary and without justification. Accordingly the judgment against the plaintiff was affirmed.—Trent v. American Service Co., 206 S. W. (2d) 301 (Tenn., 1947).

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL April 10, page 1001.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Parts I & II. Various cengers, June 21-23. Final date for filing application is May 22. Part II. Various centers, April 26-27. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2. Part III. Various centers, June. Sec., Dr. J.S. Rodman, 225 S. 15th Street, Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

American Board of Anesthesiology: Oral. New York, April 12-15, Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York 22..

American Board of Internal Medicine: Written. Oct. 18. Final date for filing application is June 1. Asst. Sec-Treas., Dr. W.A. Werrell, 1 West Main St., Madison 3, Wis.

American Board of Ophthalmology: Oral. Baltimore, May 20. Chicago, Oct. 6, Written. Various centers. Jan. 1949. Final date for filing application is July 1, 1948. Sec., Dr. S. Judd Beach, 56 Ivie Rd., Cape Cottage, Maine.

American Board of Orthopaedic Surgery: Part II. Chicago, January 1949. Final date for filing application is August 15, Sec., Dr. Francis M. McKeever, 1136 W. 6th St., Los Angeles 14.

June 15-19. Sec., D.M. Lierle, University Hospital, Iowa City.

American Board of Pediatrics: Oral. Cleveland, April 23-25. Chicago, June 25-27. Seattle, Sept. 10-12. Atlantic City, Nov. 17-19. Written. July 30. Sec., Miss Lea Leonard, 718 Royal Union Bldg., Des Moines, Iowa.

American Board of Physical Medicine: Parts I & II. Chicago, June 19-20. Final date for filing application is April 17. Sec., Dr. R.L. Bennett, 30 N. Michigan Ave., Chicago 2.

American Board of Plastic Surgery: Examinations are given in April and November of each year in the home town of applicants. Sec., Dr. Robert H. Ivy, 1930 Chestnut St., Philadelphia.

American Board of Psychiatry and Neurology: Oral. All Groups, San Francisco, October. Final date for filing application is July 15. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Surgery: Written. Part I. Oct. Final date for filing application is July 1. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia.

American Board of Urology: Chicago, Feb. 12-16, 1949. Sec., Dr. Harry Culver, Route #13, Sunnyside Rd., Minneapolis 4.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

American Journal of Clinical Pathology, Baltimore

18:1-100 (Jan.) 1948

Photo-Electric Oxyhemograph Continuous Method for Measuring Oxygen Saturation of Blood. F. W. Hartman, Vivian G. Behrmann and F. W. Chapman.—p. 1.

Hemangioma of Small Intestine with Special Reference to Intussusception: Review of Literature and Report of 3 New Cases. P. S. Hansen. —p. 14.

Elevated Serum Amylase in Alcoholics. C. A. Domzalski and B. M. Wedge.—p. 43.

Diffuse Interstitial Myocarditis in Epidemic Encephalitis. H. Ungar. —p. 48.

Case of Shigella Alkalescens Cystopyelitis and Bacteremia. L. Cardon and O. Felsenfeld.—p. 55.

Intestinal Coccidiosis: Report of 2 cases of Isospora Hominis. J. D. Kirshbaum.—p. 58.

Elevated Serum Amylase in Alcoholic Addicts.—Domzalski and Wedge cite literature to the effect that alcohol may play a role in the production of pancreatitis (pancreatic necrosis). Both patients with chronic pancreatitis recently observed at their hospital were chronic alcoholic addicts. The authors made amylase determinations on the serums of 50 alcoholic persons and of 50 nonalcoholic control patients. Elevated serum amylase was found in 12 of 50 chronic alcoholic addicts following recent alcoholic intoxication but in only 1 of 50 control patients. It is suggested that elevation of serum amylase in those with alcoholism represents evidence of subclinical pancreatitis and that this condition may be a precursor of severer clinical forms of pancreatitis.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

32:1-98 (Jan.) 1948

Minimal Infectious Inoculum of Spirochaeta Pallida (Nichol s Strain), and Consideration of Its Rate of Multiplication in Vivo. H. J. Magnuson, H. Eagle and R. Fleischman.—p. 1.

Effect of Antisyphilitic Treatment on Microscopic Appearance of Syphilitic Aortitis. B. Webster and G. G. Reader.—p. 19.

*Three Years of Penicillin Alone in Neurosyphilis. J. H. Stokes, H. P. Steiger and G. D. Gammon.—p. 28.

Study of Nutritional Requirements of Reiter Strain of Treponema Pallidum. H. R. Whiteley and C. N. Frazier.—p. 43.

Effectiveness in Experimental Syphilis of Penicillin in Peanut Oil-Beeswax Given in Sixteen Daily Injections. W. L. Fleming and Mary W. Holcombe.—p. 53.

Termination of Therapeutic Malaria with Chloroquine. R. R. Kierland and W. G. McCreight.—p. 57.

Penicillin Alone in Neurosyphilis.—The report by Stokes and his co-workers is the fourth in a series presented by the University of Pennsylvania on the treatment of neurosyphilis with penicillin alone. Since the organization of the Pennsylvania group, 1,004 patients have been treated with penicillin, of whom 422 had neurosyphilis. There are no striking differences between the effect of earlier lower and later higher dosage, nor is great additional effect secured by second and third courses. The good effect of penicillin ranges through all the categories of neurosyphilis from asymptomatic neurosyphilis to paresis. A comparison of penicillin with malaria treatment in neurosyphilis (based on the literature) indicates that in paresis penicillin "catches up" on malaria by the third year, equaling it in symptomatic improvement and producing a superior effect on the spinal fluid. In taboparesis and meningovascular neurosyphilis the results with penicillin are serologically superior and clinically equal to those with malaria. In tabes dorsalis the clinical improvement is one-third better than with malaria in the second and third years, and spinal fluid normality is obtained twice as often with penicillin as with malaria in the same period. In asymptomatic neurosyphilis the results obtained with penicillin are the best in any diagnostic category. Of 65 patients with lightning pains, two thirds showed some improvement. Of 6 patients with gastric crises, 3 showed improvement. The most important complication of penicillin therapy in neurosyphilis is the Herxheimer reaction, or therapeutic shock. Serious damage may be done by full initial dosage. Ten thousand units per injection at the start is not low enough. Five hundred units per injection, ascending to full dosage in four to five days, is being tried. A course of 9.6 million units of water-soluble penicillin on a two hour round the clock schedule covering ten to twenty days, with a full dosage level per injection of 40,000 to 80,000 units, is on trial.

Annals of Surgery, Philadelphia

127:1-192 (Jan.) 1948. **Partial Index**

*Ligation and Division of Abdominal Aorta for Metallic Embolus from Heart: Postoperative Observations of Circulation in Extremities F. W. Cooper Jr., M. H. Harris and J. W. Kahn.—p. 1.

One-Stage Resection and Anastomosis of Colon: Utilizing Furniss-Clamp. J. W. Hinton and S. A. Localio.—p. 12.

Arterial Supply of Distal Colon Pertinent to Abdominoperineal Proctosigmoidectomy with Preservation of Sphincter Mechanism. H. E. Bacon and C. H. Smith.—p. 28.

Surgical Treatment of Cardiospasm. E. B. Kay.—p. 34.

Spontaneous Rupture of Malarial Spleen: Case Report and Analysis of 64 Reported Cases. F. B Hershey and J. M. Lubitz.—p. 40.

*Penetrating Wounds of Cerebral Ventricles. H. G. Schwartz and G. E. Roulhac.—p. 58.

Homogenous Fetal Cartilage Grafts to Bone: Experimental Study. S. D. Gordon and R. F. Warren.—p. 90.

Acromioclavicular Dislocation. End-Results of Screw Suspension Treatment. B. M. Bosworth.—p. 98.

Ischemic Necrosis of Anterior Crural Muscles. G. S. Phalen—p. 112.

Obstructive Lesions of Small Intestine and Sigmoid Due to Irradiation. J. G. Spackman.—p. 121.

Prolonged Intercostal Nerve Block in Upper Abdominal Operations. S. Belinkoff.—p. 136.

Technic for Blocking Carotid Sinus Nerves. J. Pick and H. Wertheim. —p. 144.

Pancreatic Calculi. E. L. Eliason and R. F. Welty.—p. 150.

Cystadenoma of Pancreas. E. E. Jemerin and N. A. Samuels.—p. 158.

Mucocele of Appendix, with Myxoglobulosis. J. G. Probstein and G. N. Lassar.—p. 171.

Carcinoma of Breast in Absence of Clinical Breast Findings. A. S. Jackson.—p. 177.

Hamartoma of Liver. R. J. Patton.—p. 180.

Case of Glomus Tumor with Primary Involvement of Bone. R. Lattes and D. C. Bull.—p. 187.

Division of Abdominal Aorta for Embolus.—The case reported by Cooper and his associates concerned a soldier aged 22, who had sustained a penetrating wound of the left arm and chest. Roentgenograms showed a foreign body in the heart. About two months later an attack of severe, sharp, stabbing precordial pain radiating to the abdomen and region of the right hip occurred. In view of the changes in pulsations in the extremities it was believed that the pain had been produced by shifting of the bullet in the aorta or by a dissecting aneurysm of the aorta. During the following nine days the pulse in the right lower extremity varied in amplitude and that in the left was absent. Then the episode of thoracic and abdominal pain recurred. About a week later the patient complained of weakness and fatigability of both legs and coldness of the right foot. Since the patient complained of recurrent attacks of pain in chest and abdomen, it was feared that the abdominal aorta was being eroded by the foreign body. Fluoroscopic examination demonstrated motion of the foreign body, and there was evidence of peripheral vasospasm in the lower extremities from irritation of the aortic wall. An operation was planned. The conditions present gave an ideal sequence leading to ligation of the aorta. The patient was young with the vascular elasticity of youth. Occlusion of the aorta was not sudden but progressive over several weeks, with variations in the completeness of obstruction to blood flow. At the time of operative intervention the vessel had become completely occluded, with an adequate collateral circulation in the legs as manifested by the prompt rise in skin surface temperatures of the toes. Postoperatively, the distal vascular bed was relieved of vasospasm produced by the foreign body. The lower extremities reacted normally to changes in environmental temperature after aortic division.

One Stage Anastomosis of Colon.—Hinton and Localio report observations on 26 consecutive colonic resections in all regions of the colon above the peritoneal reflection, which were done in one stage without a proximal colostomy or ileostomy and were anastomosed aseptically with the aid of a Furniss

clamp. There was a single fatality, which occurred on the fifth day while the patient was returning from the lavatory. There were 3 abdominal complications. The postoperative hospital stay varied from seven to seventy-six and averaged nineteen days. Only nonobstructed patients were selected for this procedure. Five to seven days were allowed for preoperative preparation. Attempts were made to replenish the stores of tissue proteins. The patients received, per day, 2,000 cc. of "amigen," 500 mg. of ascorbic acid and 200 mg. of vitamin B complex parenterally. Anemia was corrected by transfusion of whole blood. The patient was placed on a high protein, low residue diet. Purging was carried out with magnesium sulfate. The patient received 12 Gm. of succinylsulfathiazole per day. At operation the colon was found collapsed and free from fecal material. A transfusion of whole blood was administered immediately postoperatively. A Levine tube was left in the stomach, but suction was not used. Fluids were permitted by mouth, excess gastric residue being siphoned off by the Levine tube. Nutrition was maintained by infusion of "amigen" and dextrose in distilled water. When the patient passed gas by rectum, the Levine tube was removed, parenteral feeding was gradually discontinued and oral feeding gradually liberalized. The bowels moved spontaneously between the third and fifth days. All patients were ambulated on the first postoperative day and daily thereafter. They were urged to use the bathroom facilities rather than the bedpan. Succinylsulfathiazole was used postoperatively. The authors consider aseptic anastomosis with the Furniss clamp a satisfactory and simple method.

Penetrating Wounds of Cerebral Ventricles.—The report by Schwartz and Roulhac is based on 50 consecutive cases of verified ventricular penetration. Thirteen of the penetrations were operated on primarily by the authors. Thirty-one wounds were inadequately débrided at forward installations and were reoperated by the authors one or more times because of infection or retained foreign bodies. Fourteen of these had retained bone chips or metallic foreign bodies lying within a ventricle. There were 5 cases of ventricular penetration which were operated on at other installations with recovery. Over-all mortality was 15 cases, of which 9 were due to infection and 6 to vital brain damage. Treatment of ventricular wounds is no different from that of other penetrating wounds of the brain, even though they are more serious. Patients suspected of having a ventricular wound should be given top priority for surgery, for the greater the delay the greater is the risk of infection or clot in the ventricles. The crux of the treatment of these wounds is adequate débridement of the entire tract, including the ventricle, under direct vision. Infected cases should be handled in the same way, with removal of debris, retained bone fragment: and pus, and closure of the wound. Direct instillation of penicillin at the time of operation, plus parenteral penicillin and sulfadiazine are effective only when combined with surgical measures.

Archives of Dermatology and Syphilology, Chicago

57:1-140 (Jan.) 1948

Etiology and Rehabilitation. R. M. B. MacKenna.—p. 1.
Graduate Education in Dermatology. P. A. O'Leary.—p. 11.
Survey of Pathologic Studies of Cutaneous Diseases During World War II. A. C. Allen.—p. 19.
Liquid Oxygen in Dermatologic Practice. R. L. Kile and A. L. Welsh.—p. 57.
Spindle Cell Epidermoid Epithelioma Simulating Sarcoma in Chronic Radiodermatitis. C. F. Sims and N. Kirsch.—p. 63.
Chemistry of Palmar Sweat. V. Ammonia Nitrogen. W. C. Lobitz Jr. and H. L. Mason.—p. 69.
Technic and Problems of Roentgen Ray Epilation. F. C. Combes and H. T. Behrman.—p. 74.
American Cutaneous Leishmaniasis: Report of 12 Cases from Canal Zone. J. S. Snow, E. M. Satulsky and B. H. Kean—p. 90.
Sebaceous Adenoma: Review of Literature and Report of Case. W. F. Lever.—p. 102.
Lymphogranuloma Venereum: Observations on 388 Patients at Bellevue Hospital. M. J. Costello and C. S. D'Avanzo.—p. 112.

Lymphogranuloma Venereum.—Costello and D'Avanzo report on 388 patients admitted to the dermatologic wards of Bellevue Hospital with a diagnosis of lymphogranuloma venereum in the ten year period 1936 to 1945, inclusive. Of the patients 317 were men. During the last two years there has been a decided increase in the female patients, in whom the disease was more chronic and longer duration. Nearly three fourths of the patients were Negroes, and 3 of the white men admitted sexual relations with Negro women. The authors believe that this fact might be elicited more frequently if this information were definitely sought. The average duration of the disease in patients with inguinal involvement of the lymphatic nodes previous to hospitalization was thirty and seven-tenths days, while the average duration of the disease in patients with rectal changes previous to admission to the hospital was thirty-two and two-tenths months. The genitals and the inguinal lymph nodes were primarily involved in 344. In 40 the anorectal region was involved. There were also 2 cases with involvement of the perianal region, 1 of the mandibular region and 1 of the scrotal area. An intradermal test with Frei antigen was performed in 380 of the 388 patients. Of these, 365, or 95.5 per cent, showed a positive reaction. There were 15 patients who had inguinal adenopathy for less than one week and in whom the reaction in the initial Frei test was negative. Reactions in repeated Frei tests at subsequent intervals became positive. The Frei test should be repeated several times in suspected cases of inguinal adenopathy. Before the use of sulfonamide drugs for lymphogranuloma venereum, routine treatment consisted of aspiration of the buboes and the administration of antimony potassium tartrate or stibophen. Since 1938 the sulfonamide drugs have been used, and these together with rest in bed now constitute the best treatment. Surgical intervention in the cases of early disease should be reduced to a minimum. In all cases of "inguinal abscess" and perianal infection and abscess there should be an intradermal test with Frei antigen before operative intervention is performed.

Archives of Internal Medicine, Chicago

80:697-856 (Dec.) 1947

*Fifteen Years' Experience with Free Feeding of Patients with Bleeding Peptic Ulcer: Fatal Cases. E. Meulengracht.—p. 697.
Epidemiologic Study of 757 Cases of Rheumatic Fever. R. W. Quinn.—p. 709.
Low Serum Potassium Level During Recovery from Diabetic Coma, with Special Reference to Its Cardiovascular Manifestations. M. Frenkel, J. Groen and A. F. Willebrands.—p. 728.
*Metabolic Studies in Diabetic Acidosis: I. Effect of Early Administration of Dextrose. M. Franks, R. F. Berris, N. O. Kaplan and G. B. Myers.—p. 739.
Ventricular Tachycardia and Bilateral Amaurosis Produced by Quinine Poisoning. A. H. Diamondstone, B. L. Braveman and L. A. Baker.—p. 763.
*Rheumatoid Arthritis in Children: Clinical Study. N. S. Pickard.—p. 771.
*Acute Panarteritis in Allergic Persons. J. B. Miale, K. H. Doege and M. Piehl.—p. 791.
Syphilis: Review of Recent Literature. F. W. Reynolds and J. E. Moore.—p. 799.

Bleeding Peptic Ulcer.—Meulengracht treated 1,031 patients with bleeding peptic ulcer by free feeding as a routine measure during the period June 1931 to June 1946. Death occurred in 26 patients, 17 men and 9 women, during their stay in the hospital. All except 1 of these patients were over 40 years of age and half were over 60. Many had large ulcers penetrating into the pancreas or the liver, and many had complicating diseases. If all the fatal cases are included, the gross mortality is 2.5 per cent. If cases are excluded in which death was entirely or principally due to causes other than bleeding as well as those in which the patients died twenty-four hours after admission to the hospital and therefore before they had received the treatment, the net mortality is 1.5 per cent. The risk of hemorrhage in the free feeding program is greatest in the higher age groups, presumably because of the poor condition of the vessels and the various complicating diseases in those age groups. In all the fatal cases the bleeding manifested itself as hematemesis. The latter indicates a worse prognosis than melena. A more ample use of blood transfusions is recommended in cases which threaten to terminate fatally.

Diabetic Acidosis.—Franks and his co-workers limited the intake of 28 patients with severe diabetic acidosis or coma to water, sodium chloride, dextrose and insulin supplemented in some cases by plasma, blood or alkali. Determinations of the blood sugar content, carbon dioxide combining power, chloride and inorganic phosphorus contents and hematocrit readings were made at approximately four hour intervals for twenty-four hours. Seven patients received no supplementary dextrose until the blood sugar level had fallen within the normal range. Twenty-one patients received dextrose intravenously or by mouth from the onset of therapy; 10 patients were given dextrose at

rates of 6 to 20 Gm. per hour during the first period, and dextrose was given at rates exceeding 20 Gm. per hour to 11 patients. The severity of the condition on the patient's admission to the hospital was taken as a basis for the evaluation of therapeutic results. The patients of the saline group had an average severity index of 24 per cent and an actual fatality rate of 14 per cent, while the 11 patients receiving large amounts of dextrose early had a severity index of 37 per cent and an actual fatality rate of 36 per cent. The administration of dextrose in the early hours resulted in prolonged hyperglycemia, pronounced glycosuria and polyuria. The maintenance of hyperglycemia did not accelerate the disappearance of acetone from the urine or the rise in plasma carbon dioxide combining power. The early administration of dextrose appeared to have an unfavorable influence on the outcome in the group as a whole. For further evidence the clinical analysis was extended to a total of 71 patients with diabetic coma. Sixteen of these received sodium phosphate and will be considered in another paper. For 22 of the remaining, from whom dextrose was withheld for at least the first four hours, the mean severity index was 40 per cent and the actual fatality rate was 36 per cent. The other 33 patients received dextrose during the first four hours and had a mean severity index of 37 per cent but a fatality rate of 52 per cent. These results indicate that dextrose should not be administered in diabetic acidosis until the blood sugar level has fallen within or near normal range.

Rheumatoid Arthritis in Children.—Pickard reports the end results in 35 cases of rheumatoid arthritis in children who had been followed for thre to more than five years. Etiologic factors in these cases appear to have been infection, trauma and allergy. The essential feature of the disease is an altered specific reaction of the patient to these activating agents. There is essential agreement with the conclusion of Colver that the disease is self limited. There is essential disagreement with the same author in regard to the "second attack" or recrudescence after quiescence. After the involvement of various joints by the rheumatoid process, a wide difference in the outcome may be anticipated according to the joint involved, with poorest results in the elbows, the carpal joints and the wrists and relatively good in the ankles and the knees. Visceral lesions accompany the severe forms of the disease; "rheumatism-like" lesions in the heart and amyloid degeneration in the liver and spleen are of greatest importance. A persisting monarticular form of rheumatoid arthritis in children may be observed at times and is difficult to distinguish in some cases from tuberculous synovitis. Rheumatoid arthritis and rheumatic fever may closely resemble one another. There is a reasonably good basis for the removal of focal infection during the active phase of the disease. Surgical attack on joints during the active phase of the disease does not seem advisable. The incidence of recovery is high if all cases are taken into consideration; 3 patients died, 11 were left with residual crippling of various degree and 14 recovered without residual crippling. In 7 patients the disease was still active at the time of last observation.

Panarteritis in Allergic Persons.—Miale, Doege and Piehl report the occurrence of acute necrotizing arteritis in 2 men, aged 40 and 67, respectively, who both had definite atopy. The first patient had gangrene of the ileum with acute allergic dermatitis on the basis of an acute arteritis. The evidence of acute renal damage coincident with the abdominal condition, plus the residual renal damage demonstrated by a phenol-sulfonphthalein test of renal function suggested that there was simultaneous arterial involvement in the kidneys and possibly in other organs. The condition was diagnosed early in the course of the illness, all medication stopped and a good recovery made. The second patient died, and final diagnosis on necropsy was visceral angiitis (panarteritis), glomerulonephritis on the basis of visceral angiitis, pleural adhesions, hydrothorax, ascites, fibrous obliterated pericarditis and passive congestion of the lungs, spleen and liver. The vascular necrosis was severest in the kidneys and liver. Previous to the fatal disease the patient had been seen many times in the dermatologic department because of severe asthma and allergic dermatitis. In these 2 cases there is enough evidence to show that the relationship between hypersensitivity and acute arterial disease is more than accidental. In case 1 all medication was stopped as soon as the diagnosis was made in the hope that the antigen might be excluded by such means. This may be a lifesaving measure when the antigen is exogenous. The authors feel confident that more and more cases will be recognized before autopsy is performed. New developments in the field of the antiallergic drugs may lead to a more active method of therapy in the near future.

Archives of Neurology and Psychiatry, Chicago

58:653-788 (Dec.) 1947

Central Nervous System in Pneumonia (Nonsuppurative Pneumonic Encephalitis): III. Experimental Study. H. H. Noran, A. B. Baker and W. P. Larson.—p. 653.
Ballism and Subthalamic Nucleus (Nucleus Hypothalamicus; Corpus Luysi): Review of Literature and Study of 30 Cases. J. R. Whittier. —p. 672.
Electroencephalographic Studies on Induced and Excised Epileptogenic Foci in Monkeys. B. L. Pacella, Lenore M. Kopeloff and N. Kopeloff. —p. 693.
Investigations on Narcodiagnosis. F. A. Freyhan.—p. 704.
Postoperative Period of Survival of Patients with Oligodendroglioma of Brain: Report of 25 Cases. H. A. Shenkin, F. C. Grant and J. H. Drew.—p. 710.
*Significance of Changes in Electrocardiogram After Electrically Induced Convulsions in Man. M. D. Altschule, W. M. Sulzbach and K. J. Tillotson.—p. 716.
Spatial Organization of Visual Perception Following Injury to Brain. M. B. Bender and H. L. Teuber.—p. 721.
*Poliomyelitis: Study of Epidemic of 40 Cases in Key West, Fla. May-August 1946. W. D. Davis and C. M. Silverstein.—p. 740.

Electrocardiographic Changes in Electric Convulsions.—Altschule and his associates made electrocardiographic studies on 10 patients, who were treated with electrically induced convulsions. Five patients were studied once or twice and the other 5 were studied four to seven times each. Observations made on these patients corroborate the previously recorded shifting of the site of origin of the heart beat, as evidenced by pronounced sinus arrhythmia, periods of sinus bradycardia, frequent auricular and nodal premature beats and, in 1 instance, auricular tachycardia. This type of disturbance in cardiac rhythm is a consequence of vagal hyperactivity. The increase in vagal activity usually does not induce sufficient cardiac inhibitation to cause more than transitory bradycardia; the systemic circulation is not slowed; the occurrence of vagal arrhythmia goes with other evidences of antonomic stimulation exhibited by patients during and after convulsive seizures.

Poliomyelitis in Key West.—Davis and Silverstein report observations they made in the course of an epidemic of poliomyelitis which began on the island of Key West in May 1946. The population of Key West at the time of the epidemic was about 14,000 civilians and about 3,500 naval personnel and their families. There were 40 verified cases of poliomyelitis and 190 cases of suspected and probable abortive poliomyelitis. There were 7 pregnant women with poliomyelitis; 6 of them had the paralytic form. Nearly three fourths of the patients in Navy families were adults (19 to 33 years of age), whereas only 10.5 per cent of the civilian patients were adults. There were three instances in which 2 verified cases occurred in the same family (6 patients). Thirteen of the remaining 34 patients

gave a history of a febrile illness resembling poliomyelitis in one or more of the family at the same time. Eight patients had a normal temperature on admission. Since fever is usually a cardinal sign of infection, a patient suspected of having poliomyelitis who has no fever, but mild symptoms, should be asked routinely about recent fever or should be watched for the subsequent development of fever. A history of direct contact with persons known to have poliomyelitis was obtained for 18 (almost one-half) of the patients. Polluted beach water and flies were also possibly incriminated in the transmission of the virus. The treatment was that followed by the Georgia Warm Springs Foundation with regard to general nursing care, use of hot packs, baths and passive motion, reeducation of muscles and prolonged observation and treatment after the acute stage of the disease.

Arizona Medicine, Phoenix

5:1-124 (Jan.) 1948

Virus Pneumonia. W. B. Yegge.—p. 31.
Clinical Aspects of Bronchial Asthma, Diagnosis and Treatment. F. B. Schutzbank.—p. 38.
Hypertrophic Pyloric Stenosis and Vomiting in Infancy. D. E. Nelson. —p. 44.
Medical Observations on Management of Shock. C. A. L. Stephens Jr. —p. 50.
Torsion of Spermatic Cord in Left Inguinal Canal in Cryptorchid. C. E. Yount, E. A. Born and C. E. Yount Jr.—p. 54.
Hydatidiform Mole Followed by Chorionepithelioma. C. B. Warrenburg. —p. 57.
Malicious Poisoning of Water Supplies and Its Detection. R. A. Greene and E. L. Breazeale.—p. 60.
Forcing Socialized Medicine on America by Use of Federal Employees and Government Money. F. A. Harness.—p. 64.
Changing Trends in Medical Research and Practice. E. F. Boyd.—p. 71.

Canadian Medical Association Journal, Montreal

58:1-114 (Jan.) 1948

Treatment of Acute Perforated Peptic Ulcer. D. L. C. Bingham.—p. 1.
Refrigeration Anesthesia. Ethel A. Noble.—p. 5.
Surgical Treatment of Congenital Heart Disease: (Tetralogy of Fallot). G. Murray.—p. 10.
Examination of the Hard of Hearing. E. E. Scharfe, G. E. Hodge and T. Cadman.—p. 12.
Control of T.N.T. Sickness in Industry. W. E. Park.—p. 19.
Treatment of Certain Psychoneuroses by Modified Insulin Therapy. M. Carnat, F. J. Edwards and Elizabeth I. Fletcher.—p. 22.
*Bronchogenic Carcinoma: (Twelve Year Review and Operative Results). E. D. Gagnon.—p. 25.
Carcinoma of Urethra in Female. M. Seng and M. Siminovitch.—p. 29.
*Cervical Herniation of Lung. J. F. Meakins, C. J. Wyatt and M. Aronovitch.—p. 33.
Management of Late Toxemias of Pregnancy. J. L. MacArthur.—p. 35.
Treatment of Peptic Ulcer. A. H. Gordon.—p. 38.
Incoordinate Uterine Action in Labor. T. N. A. Jeffcoate.—p. 42.
Anesthesia for Intracranial Operations. A. R. Hunter.—p. 48.
Accidental Hemorrhage. G. F. Gibberd.—p. 53.
Dupuytren's Contracture. R. G. Langston and E. J. Badre.—p. 57.
Field Surgical Unit. J. A. Hillman.—p. 61.
Subdural Hematoma in Infancy. T. Statten.—p. 63.

Bronchogenic Carcinoma.—Gagnon says that from 1934 to 1945, inclusive, 508 patients with bronchogenic carcinoma were admitted to the Toronto General Hospital. He excludes from consideration 284 patients in whom the diagnosis appeared obvious from clinical examination or after biopsy from secondarily involved glands or skin. In the 224 patients forming the basis of this review, the diagnosis was determined by microscopic examination of tumor tissue obtained either by bronchoscopy, thoracotomy, biopsy or necropsy. The increase is apparent and can probably be explained by increasing awareness on the part of physicians, which leads to a more frequent recognition. The disease is much commoner in the male, there being only 25 females in this series. The oldest patient was 84 and the youngest, 15. The majority of patients were between the fourth and sixth decades of life. Bronchoscopy permitted a positive diagnosis in 69.1 per cent of those examined by this means. The disease is somewhat more frequent on the right side than on the left side. Eighty-six chests were opened and resection was completed in 49 cases, 5 of which were lobectomies. Operative mortality for lobectomy is nil; the maximum survival was nine months. Operative mortality following pneumonectomy in the series was 36 per cent, though for the last year of the review it was only 25 per cent. In 1946 the mortality was further reduced to 6.6 per cent. One fourth of all patients on whom pneumonectomies were performed are alive today and apparently free of disease, their survival ranging from seven months to eight and one half years.

Cervical Herniation of Lung.—Meakins and associates state that herniation of the lung is rare, only 200 cases having been recorded in medical literature. The authors differentiate between cervical, thoracic and diaphragmatic hernia. They quote Maurer and Blades as saying that "cervical hernias usually occur through the superior aperture of the thorax in the interval between the sternocleidomastoid and scalenus anticus muscles following some tear or deficiency in Sibson's fascia which normally limits the cervical excision of the dome of the pleura." The authors report 2 cases of cervical hernias of the right lung. First, a man aged 58 had a multiplicity of lesions, including carcinoma of stomach and duodenum. Necropsy confirmed these lesions as well as herniation of the apex of the right lung. The herniation could have been due to a congenital structural defect in the apical and cervical area. In view of the clearcut history of injury to the affected area with the immediate appearance of the bulge one can assume that in this case trauma was probably the originating factor. Injury could have been superimposed on congenital weakness. The second case concerned a man aged 53. In this case there was strong evidence that trauma was the etiologic factor.

Georgia Medical Association Journal, Atlanta

37:1-38 (Jan.) 1948

Sickle Cell Anemia and Pregnancy: Report of Case. J. C. Neal, V. P. Sydenstricker and R. Torpin.—p. 1.
Observations on Prison Psychoses. M. M. Estes and J. S. New .—p. 2.
Narcohypnosis in Medical Practice. H. R. Lipton and J. K. Fancher. —p. 6.
Chronic Alcoholism. J. D. Campbell.—p. 12.
Dynamics of Pathologic Depression. L. F. Woolley.—p. 16.
Subacute Bacterial Endocarditis: Report of Patient Treated with Massive Doses of Penicillin. W. J. Nelson, W. J. Gower and E. A. Allen. —p. 23.
*Use of Radium in Nasopharynx for Deafness and Its Clinical Effects: Report of Cases. J. L. Jennings.—p. 24.

Use of Radium in Nasopharynx.—Jennings used radium in the nasopharynx by means of a nasal applicator which was designed by Drs. Crowe and Burnam. A capsule of "monel" metal containing 50 mg. of radium sulfate measures 15 mm. in length, has an inside diameter of 1.7 mm. and a wall 0.3 mm. thick. This allows the beta rays to penetrate 3 mm. of tissue. Indications for the use of radium in the nasopharynx are: blockage of the eustachian tube by lymphoid tissue; the presence of lymphoid tissue in the nasopharynx in conjunction with nasal allergy, postnasal discharge, frequent colds and aero-otitis, and also a small area of lymphoid tissue in the nasopharynx which harbors infection and sensitizes the patient. The radium applicator is allowed to stay in place for twelve minutes and then is transferred to the opposite side of the nose for the same period of time. The treatment is carried out at two to three weeks' intervals for three to four applications of radium. At times it is wise to remove the large mass of adenoids surgically before radium therapy. This eradicates the small remnants of adenoid tissue possibly not removed at the surgical procedure. With this method it is possible to eliminate in six months the lymphoid tissue which may require ten to twelve years for removal by natural atrophy. The author cites encouraging results obtained with radium in asthma and allergic conditions and in earache without discharge, but he admits that not all patients are relieved or improved.

Indiana State Medical Assn. Journal, Indianapolis

41:1-184 (Jan.) 1948

Effect of Taxes on Your Estate Plans. B. B. Emswiller and A. Stump —p. 21.
Indiana's Licensed Nursing Homes. O. F. Walls.—p. 25.
Indiana Vocational Rehabilitation: Its Organization, Scope and Services F. M. Hall.—p. 32.
Home Town Medical Care Program of Veterans Administration. C. F Thompson.—p. 35.
Federal Income Tax and Medical Profession. F. S. Wilcox.—p. 36.
Trends in Medicine. R. L. Sensenich.—p. 77.
Planned Parenthood—Road to National Health and World Peace. C. O. McCormick.—p. 81.

Journal of Experimental Medicine, New York

87:1-86 (Jan.) 1948

Preparation from Human Red Cells of Substance Inhibiting Virus Hemagglutination. P. M. deBurgh, P.-C. Yu, C. Howe and M. Bovarnick.—p. 1.
Studies on Endemic Pneumonia of Albino Rat: III. Carriage of Virus-Like Agent by Young Rats and in Relation to Susceptibility. J. B. Nelson.—p. 11.

*Studies of Distribution of Poliomyelitis Virus: V. Virus in Familial Associates of Cases. G. C. Brown, T. Francis Jr. and J. Ainslie. —p. 21.
Studies on Plant Hypertensinase. F. Gollan, Evelyn Richardson and H. Goldblatt.—p. 29.
Studies in Relation of Hemolytic Streptococcus to Rheumatic Fever. T. N. Harris.—p. 41.
Heparinemia(?) An Anticoagulant in Blood of Dogs with Hemorrhagic Tendency After Total Body Exposure to Roentgen Rays. J. G. Allen, Margaret Sanderson, Mary Milham and others.—p. 71.

Poliomyelitis Virus in Familial Associates.—Brown and his collaborators in order to ascertain the role of the familial associate as a healthy carrier or a possible source of infection of poliomyelitis made studies on four families. Two criteria were required: first, that the family include at least two children other than the one with poliomyelitis; second, that collection of specimens could be started within three days of onset of illness in a member of the family. The occurrence and duration of the carrier state in familial associates of those with recognized cases of poliomyelitis was studied by the examination for virus of stool specimens collected from the members of the four families at regular intervals for a period of over two months. The results indicate that virus may persist in their stools continuously for four to five weeks; virus may be encountered intermittently in the stools; in some instances virus may be present for brief periods only; children are more likely to maintain virus than are adults in the same family; infection of a family takes place rapidly, suggesting simultaneous infection from a common source.

Journal Industrial Hygiene & Toxicology, Baltimore

30:1-70 (Jan.) 1948

Acute Toxicity of Ethylene Imine to Small Animals. C. P. Carpenter, H. F. Smyth Jr. and C. B. Shaffer.—p. 2.
Comparison of Acute Toxicities of Ethylene Imine and Ammonia to Mice. S. D. Silver and F. P. McGrath.—p. 7.
*Toxicologic Studies on Laboratory Animals of Certain Alkyld. nitrophenols Used in Agriculture. H. C. Spencer, V. K. Rowe, E. M. Adams and D. D. Irish.—p. 10.
Antimony Trisulfide. F. M. R. Bulmer and J. H. Johnston.—p. 26.
Air Contamination During Machining of Beryllium Stainless Steel. A. C. Titus.—p. 29.
Proteinuria and Kidney Injury Among Workmen Exposed to Cadmium and Nickel Dust: Preliminary Report. L. Friberg.—p. 32.
Two Outbreaks of Carbon Disulfide Poisoning in Rayon Staple Fiber Plants in Poland. E. A. Paluch.—p. 37.
Study of Health Hazards of Tobacco Stemming and Redrying Industry. W. E. McCormick, Maxine Smith and S. P. Marsh.—p.43.
Tellurium: III. Toxicity of Ingested Tellurium Dioxide for Rats. R. H. De Meig and W. W. Jetter.—p. 53.
*Determination of Lead in Freshly Voided Urine: Rapid Screening Test. J. Cholak, D. M. Hubbard and R. E. Burkey.—p. 59.
Further Experience with Range Finding Test in Industrial Toxicology Laboratory. H. F. Smyth Jr. and C. P. Carpenter.—p. 63.

Toxicologic Studies on Alkyldinitrophenols Used in Agriculture.—Spencer and his co-workers say that the dinitrophenols have been used for decades for the control of mites, aphids, scale insects and other pests. During the last ten years 2-cyclohexyl-4,6-dinitrophenol and its compound with dicyclohexylamine have gained wide acceptance as insecticides in greenhouse, field and orchard. Experimental work was undertaken in order to obtain toxicologic information on the hazard associated with the use of the dinitrophenols. Experiments were made on rabbits and guinea pigs. Contact with the dinitrophenols incident to their use in agriculture does not present a significant problem from cutaneous irritation. The infrequent person who is hypersensitive to this class of compounds should not work with these materials. The systemic toxicity of the dinitrophenols is sufficiently high that any one of them may present a health hazard from the inhalation of dusts or sprays. The inhalation of either liquid or dry mix concentrates (greater than 5 per cent) of any of these compounds should be avoided. In some cases respirators may be necessary. Low concentrations of the dinitrophenols are commonly found in preparations ready for field use, but reasonable care should be taken to avoid breathing excessive amounts of the dust or spray. The oral intake of the dinitrophenols should not present a problem. Care should be taken to wash well before eating. No significant health problems have arisen from residues remaining on fruits and vegetables. There is usually ample time for the removal of the residue before harvest by volatilization and by the leaching action of rain.

Determination of Lead in Urine.—Cholak and his associates point out that there has long been a need for a rapid analytic method which can be relied on to separate persons who have been subjected to hazardous lead exposure from those whose exposure to lead has been negligible or within safe limits. Such a screening test, as applied to freshly voided samples of urine, is described in detail. The method has been designed to require a minimum of equipment and manipulation and, once standardized, can easily be carried out by a well trained laboratory technician. The method is offered with the warning that although it is capable of the accurate determination of lead if followed faithfully, it does not distinguish between lead and bismuth, and therefore any results indicative of abnormal absorption of lead must be checked by the use of a more specific and precise method.

Journal of Nervous and Mental Disease, New York

106:513-618 (Nov.) 1947

*Electroencephalographic Changes Induced by Water Intoxication. R. Cohn, L. C. Kolb and D. W. Mulder.—p. 513.
Some Electro-Encephalographic Findings in Subcortical and Hypothalamic Lesions. M. W. Laufer.—p. 527.
Blocking of Chemical Decerebration by Pontile Pathology: Case Report. Barbara S. Lipton.—p. 537.
Study of Carbonic Anhydrase in Thirty-Seven Brains with Reference to Symmetry of Distribution. Winifred Ashby and D. Weickhardt. —p. 540.
Objective (Behavioristic) Criteria of Recovery from Neuropsychiatric Disorders. K. R. Eissler.—p. 550.
Observations on Emotional Currents in Interview Group Therapy with Adolescent Girls. H. Spotnitz.—p. 565.
Diary of War Neurosis. R. L. Stern.—p. 583.
Mental Hospitals: Today and Tomorrow. P. W. Thomas.—p. 587.

Electroencephalographic Changes in Water Intoxication.—Cohn and his co-workers employed the pitressin hydration test in 23 young white men, all in naval service, who were admitted to the hospital for study following one or more attacks of syncope, transitory impairment of consciousness or convulsion. The illness presented by the group was unusual, first, in the relative infrequency of the attacks and second, in the short duration of the disease. The authors observed that water intoxication gave rise to low frequency activity in the electroencephalogram in nearly all the subjects. The bioelectric changes were similar to those produced by insulin-induced hypoglycemia and oxygen poisoning. The authors conclude that the pitressin water test is not a specific test for epilepsy. They think that water intoxication, in common with hypoglycemia and oxygen metabolism collapse, is probably a phenomenon of intraneuronal dysfunction. In certain epileptic persons a positive water balance apparently disturbs already poorly functioning neurones, as determined by the electroencephalographic low frequency activity, and thereby acts as the detonating mechanism for the convulsive discharge. The absence of abnormal cerebral electric activity in water intoxication does not indicate that the observed patient does not have clinical epilepsy. In the types of patients in the study, the pitressin hydration test is of limited value for the diagnosis of epilepsy.

Journal of Pharmacology & Exper. Therap., Baltimore

92:1-102 (Jan.) 1948. Partial Index

Action of Pyridine and Some Derivatives of Pyridine-3-Carboxylic Acid on Neuromuscular Transmission. F. Valenzuela and F. Huidobro. —p. 1.
Determination of Therapeutic, Irregularity, and Lethal Doses of Cardiac Glycosides in Heart-Lung Preparation of Dog. A. Farah and G. Maresh.—p. 32.
Absorption, Distribution and Excretion of Streptomycin E. K. Marshall Jr.—p. 43.
Metabolic Fate of Chloral Hydrate. T. C. Butler.—p. 49.
Influence of Atropine and Scopolamine on Central Effects of DFP (Di-Isopropyl Fluorophosphate W. C. Wescoe, R. E. Green, B. P. McNamara and S. Krop.—p. 63.
Influence of Sulfhydryl Compounds on Diuresis and Renal and Cardiac Circulatory Changes Caused by Mersalyl. A. Farah and G. Maresh. —p. 73.
Effects of Single Doses of 6-Dimethylamino-4-4-Diphenyl-3-Heptanone (Amidone, Methadon, or "10820") on Human Subjects. H. Isbell, Anna J. Eisenman, A. Wikler and K. Frank.—p. 83.
Biological Assay of Histamine and Diphenhydramine Hydrochloride (Benadryl Hydrochloride). G. Chen, C. R Ensor and Isabel G. Clarke.—p. 90.

Kansas Medical Society Journal, Topeka

48:537-580 (Dec.) 1947

Inquiry Into Causes for Bleeding From Uterine Myomata. L. D. Odell and J. Scott.—p. 537.
Evaluation of Cardiac Patients for Surgery. M. H. Delp.—p. 540.
Acne Vulgaris. R. L. Sutton Jr.—p. 545.
Observations of Traumatic Rupture of Spleen: Report of Case. J. E. Lamy and F. A. Rieke.—p. 550.

Medical Annals of District of Columbia, Washington

16:651-726 (Dec.) 1947

Medical Statesmanship. E. L. Bortz.—p. 651.
Varicose Veins and Varicose State. J.J.Weinstein and P. B. Hudson. —p. 657.
Clinical Examination in Recognition of Heart Disease. B. Manchester. —p. 667.
General Review of Allergy. G. T. Brown.—p. 675.

17:1-70 (Jan.) 1948

Experimental Trends in Antibiotics. P. A. Bunn.—p. 1.
Penicillin. Review of Basic Principles and Their Clinical Application. H. L. Hirsh.—p. 7.
*Treatment of Bacterial Endocarditis with Penicillin and Streptomycin W. W. Zeller, H. L. Hirsh, H. F. Dowling and others.—p. 21.
*Hemorrhagic Gangrenous Exfoliative Dermatitis Following Penicillin in Oil and Beeswax: Combined Immediate and Delayed Reactions: Report of Case. J. L. Derzavis and J. Beinstein.—p. 32.
Temporal Arteritis. Critical Review of Proven Cases with Report of Additional Case with Pernicious Anemia. M. Protas and A. G. Saidman.—p. 34.

Penicillin and Streptomycin in Bacterial Endocarditis.—Zeller and his associates treated 42 patients with bacterial endocarditis by means of penicillin and 1 patient with penicillin and streptomycin. Sixteen patients died, 14 from active infection and 2 of heart failure after the infection was apparently cured. Problems concerning the use of penicillin in the treatment of bacterial endocarditis are outlined and discussed. A plan for management of patients with bacterial endocarditis is recommended.

Exfoliative Dermatitis Following Penicillin.—Derzavis and Beinstein report the case of a man, aged 56, who received one intramuscular injection of 300,000 units of penicillin in an oil and beeswax vehicle for treatment of traumatic cellulitis of the right ring finger and regional epitrochlear lymphadenitis. Within six hours he experienced severe generalized itching. On the following day there was an acute erythematous macular and maculopapular eruption over all the extremities and genitalia. During the next four days the eruption progressed through a vesicular stage in these regions followed by the appearance of hemorrhagic vesicles on the legs and thighs and a few scattered hemorrhagic vesicles on the trunk, accompanied by bullous lesions in the intertriginous areas. The peak of the dermatosis was apparently reached between the fifteenth and twentieth days, and gradual subsidence followed during the next fortnight with healing of all lesions and exfoliation of almost the entire skin in extensive keratinous sheaths. There was no reaction when the patient partook freely of peanuts and honey. The mechanism of allergic reaction to penicillin is interesting in this case because of the moderate dermatophytosis present and the severe local reaction in those regions about the toewebs. The authors cite experimental studies by other investigators that suggest the possibility of sensitization to penicillin on the basis of cross sensitization to superficial fungous diseases. Physicians should realize that penicillin is not a reactionless drug.

New England Journal of Medicine, Boston

238:1-36 (Jan.) 1948

*Anticoagulant Treatment of Postoperative Venous Thrombosis and Pulmonary Embolism. J. A. Evans and J. F. Dee.—p. 1.
Thiouracil and Allied Drugs in Hyperthyroidism. E. C. Bartels.—p. 6.
Neurologic Disturbances with Folic Acid Therapy. P. F. Wagley.—p. 11.
Lipemia Retinalis: Report of Case. S. Stearns, E. Friedman, M. Lugitch and S. H. Hoffman.—p. 16.
Toxemias of Pregnancy. B. Tenney Jr.—p. 18.
Hepatoma, with Extension Into Portal and Hepatic Veins, Inactive Portal Cirrhosis of Liver.—p. 25.
Ewing Sarcoma of Sacrum.—p. 28.

Anticoagulants in Venous Thrombosis.—According to Evans and Dee "dicumarol" has provided since April 1941 the predominant method of therapy at the Lahey Clinic. In the majority of cases a combination of heparin and "dicumarol" has been used. During the first four years heparin was given by continuous intravenous drip to cover the latent period of "dicumarol." For the past two years deep injections of heparin in Pitkin menstruum have been given subcutaneously. Evans and Dee review results obtained in 184 cases of postoperative venous thrombosis with or without pulmonary embolism during the five years 1942 to 1946. Sixty-three patients received heparin intravenously. Fifty-five received heparin in Pitkin menstruum. One to five injections of heparin in Pitkin menstruum were necessary according to the patient's refractoriness to "dicumarol." To the 184 cases must be added 54 in which patients with postoperative pulmonary embolism died untreated, because such deaths either occurred suddenly or were unrecognized as thrombosis with embolism. This makes a total of 238 cases of thromboembolic disease, or an incidence of 0.42 per cent among approximately 56,000 major surgical operations. There were 6 fatal cases in the series of 184. Two were postoperative chemical deaths. One patient early in the series died of hemorrhage from "dicumarol" poisoning. This leaves 3 fatal cases of thromboembolic disease. These 3 deaths occurred in the particularly dangerous groups of cases in which the patients had already suffered one pulmonary embolism. On analysis, none of these 3 cases presented a clearcut argument against the efficacy of anticoagulation therapy. Since 85 per cent of patients with fatal pulmonary emboli give warning signs, usually a low temperature and tachycardia or a history of previous thromboembolic disease, or have varicose veins, a plea is made for better prophylaxis. This can be accomplished by leg exercises, bandaging of limbs, early ambulation prophylactic ligation in debilitated patients over 60 years of age or the administration of "dicumarol" on the fourth day after operation.

238:37-72 (Jan. 8) 1948

Certain Public-Health Aspects of Infectious Diseases. T. M. Rivers. —p. 37.
"Fever of Unknown Origin" Due to Lymphogranuloma Venereum: Report of Case with Diagnosis by Use of Quantitative Complement-Fixation Tests. N. M. Luger.—p. 44.
Disabled Veterans of World War II: Analysis of 600 Cases Examined at Harvard University. A. Thorndike.—p. 48.
*Toxic Effects of Gases and Vapors: Mechanism of Poisoning by Volatile Solvents. M. Clinton Jr.—p. 51.
Radiation Therapy. S. A. Robins, B. E. LeVine and G. White.—p. 55.
Carcinoma of Breast; Metastases to Mediastinal Lymph Nodes Involving Esophagus and Right Main Bronchus.—p. 60.
Epidermoid Carcinoma of Bronchus of Right Lower Lobe. Bronchiectasis. —p. 63.

Toxic Effects of Gases and Vapors.—Clinton thinks that many illnesses resulting from the inhalation of toxic gases or vapors are ascribed to other causes, because the syndrome produced may resemble in every particular one of several common organic diseases. The patient is frequently not aware that the air he is breathing contains a noxious agent and fails to associate the breathing of some odd smelling but essentially nonirritating air with the occurrence of illness ten days or two weeks later. The author presents some of the basic principles involved in the absorption of toxic gases and vapors with a diagram of representative respiratory patterns of a person exposed to a thousand parts of ammonia per million parts of air and of a person exposed to ten thousands parts of trichlorethylene per million parts of air. Carbon disulfide and benzene no longer menace the health of workers as they did ten or twenty years ago, since the hazards are recognized and controlled. However, new solvents and volatile chemicals, some of which may be capable of causing serious illness, are constantly being introduced in industry and to a lesser extent turned loose on an unsuspecting public. Disease of the liver or impairment of blood cell formation has long been associated with exposures to solvent vapors. The possibility of a toxic exposure is therefore usually thought of and investigated in patients with unexplained jaundice or with anemia or leukopenia. Many exposures to toxic vapors may fail to result in either of these reactions but may cause a nephritis that clinically is readily mistaken for ordinary glomerular nephritis. Many physicians are not aware of the frequency of toxic nephritis due to exposures to toxic chemicals and may fail to inquire about such exposure in a patient with renal disease, although they would seek to determine such exposure in a patient with anemia or evidence of seriously impaired hepatic function.

Rocky Mountain Medical Journal, Denver

45:1-96 (Jan.) 1948 **Partial Index**

Modern Surgical Methods in Management of Osteomyelitis. G. J. McKelvey.—p. 21.
Surgical Treatment of Peptic Ulcer with Report of 32 Vagotomies. D. B. Seabrook.—p. 26.
Surgical Treatment of Large Colonic Cancers Which Have Secondarily Invaded Surrounding Structures. R. E. Benson.—p. 32.
Back to Basic Principles in Management of Functional Uterine Bleeding. C. A. Carmichael.—p. 37.
Diagnosis and Treatment of Coronary Heart Disease. F. R. Scheman. —p. 46.
Study of Tuberculosis Patients in Colorado Sanatoria and Their Rehabilitation Needs. E. N. Chapman and Helen E. Wilson.—p. 50.

Book Notices

What You Can Do for High Blood Pressure. By Peter J. Steincrohn, M.D., F.A.C.P. Cloth. Price, $2.50. Pp. 191. Doubleday & Co., Inc., Garden City, N. Y., 1947.

It is difficult for a physician, in writing a book of medical advice for laymen, to avoid the pitfalls of being too technical or too condescending and of magnifying or minimizing symptoms unduly. In his book Dr. Steincrohn has succeeded well in keeping to the safe middle ground. In a chatty, friendly manner he discusses the influence of the emotions on blood pressure and suggests ways by which an individual can learn to control his frame of mind at least to some extent.

Most experienced physicians will agree emphatically with the author's opening statement that "more persons are concerned about the actual height of their blood pressure than with the potential dangers of the atomic bomb." They will also agree with him that "patients have become too conscious of numerals as related to blood pressure." It is unfortunate that so many persons with elevated blood pressures believe that they must have their pressure read at frequent intervals. Dr. Steincrohn pertinently says that if all physicians would stop telling patients how high their pressure is, and if all patients would stop asking, a turning point in the treatment of hypertension would be reached.

Dr. Steincrohn does not pretend to have a magic formula for reducing blood pressure but stresses the importance of keeping one's temper, of securing enough rest and sleep, of keeping one's weight within normal limits and of avoiding overexertion. Little is said about drugs, unless alcohol be considered as such. Evidently Dr. Steincrohn agrees with the late Lewellys Barker's epigram that a man is a fool if he drinks before he is 50, but a greater fool if he does not drink after that age. "A good rule is no alcohol for the intemperate, but a spot of liquor at night for those who can take it or leave it."

This book can be read by the average hypertensive patient—and by his doctor—with profit.

Neuropathology in Its Clinicopathologic Aspects. By I. Mark Scheinker, M.D., Assistant Professor of Medicine (Neurology) and Instructor in Neuropathology, University of Cincinnati College of Medicine, Cincinnati. With a foreword by Tracy J. Putnam, M.D., Professor of Neurology and Neurological Surgery, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $6.75. Pp. 306, with 208 illustrations. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1947.

The material in this book is excellent and is presented in an easily understandable way. The subject matter on pathology is closely integrated with the clinical symptomatology and this makes the book desirable to have for ready reference. There are nine chapters on diseases of vascular origin, neurosyphilis, demyelinating processes, inflammatory diseases, myopathies, syringomyelia, cerebellar disorders, progressive degenerative diseases and presenile and involutional senile degeneration. This book is recommended to all medical students, practitioners of medicine and neuropsychiatrists. It has a fairly large bibliography.

Tropical Nutrition and Dietetics. By Lucius Nicholls, M.D., B.C., B.A., Director of Bacteriological and Pasteur Institutes, Colombo, Ceylon. Second edition. Cloth. Price; $7.50. Pp. 370, with 47 illustrations. Bailliere, Tipdall and Cox, 7 and 8 Henrietta St., Covent Garden, London, W. C. 2, 1945.

This enlarged edition has been revised to include the more recent knowledge of nutrition. It is planned primarily for workers in tropical regions and is a reflection of conditions and practices in Ceylon and the East. The initial chapters deal with the physiology and chemistry of the basic food substances. This section is followed by detailed consideration of the individual vitamins, with useful tables of food sources and available quantities. There is a useful and extensive list of foodstuffs, including fruits and vegetables, with the corresponding energy, mineral, thiamine, vitamin A and ascorbic acid values. A brief chapter on insect pests of stored cereal and pulses is useful for the tropical worker. The treatment of the subject matter and the content of the text as a whole is oriented to the practitioner.

America's Needs and Resources: A Twentieth Century Fund Survey Which Includes Estimates for 1950 and 1960. By J. Frederic Dewhurst and Associates. Cloth. Price, $5. Pp. 812, with 42 illustrations. The Twentieth Century Fund, Inc., 330 W. 42d St., New York 18, 1947.

This book is a one volume encyclopedia of the economy of the United States. Within its pages are marshaled all the salient facts of our economic life: current trends, war lessons, the nature of needs and the dimensions of the resources with which they can be met. To this the authors have added their guesses of what our economy can produce in 1950 and in 1960.

For these guesses the book is most in demand. The authors are careful to say that theirs is no "plan" or prediction of what will happen; rather it is an estimate of what can happen in our economy if each sector functions as well in the future as it has at any time in the recent past.

Consumer requirements are discussed in nine major categories, of which medical care is one. The authors of this section—both employees of the Social Security Administration—emphasize that needs for medical care will best be satisfied by improved organization of medical services; they specify group practice as an example of this.

The volume omits consideration of the effects of continuing shipments of relief supplies to foreign countries and of the possibility of another "great depression."

Practical Clinical Psychiatry. By Edward A. Strecker, A.B., A.M., Sc.D., Professor of Psychiatry, School of Medicine, University of Pennsylvania, Philadelphia; Franklin G. Ebaugh, A.B., M.D., Professor of Psychiatry, University of Colorado School of Medicine, Denver, and Jack R. Ewalt, M.D., Professor of Neuro-Psychiatry; Director, Galveston State Psychopathic Hospital, University of Texas Medical Branch, Galveston. Section on Psychopathologic Problems of Childhood by Leo Kanner, M.D., Associate Professor of Psychiatry, Johns Hopkins University School of Medicine, Baltimore. Sixth edition. Cloth. Price, $5. Pp. 476. The Blakiston Co., 1012 Walnut St., Philadelphia 5, 1947.

This sixth edition of "Practical Clinical Psychiatry" is the best to date published by the authors. There are fourteen chapters starting with personality development and function followed by methods of psychiatric examination, the organic reaction types, toxic psychosis, the affective and schizophrenic reaction types, constitutional psychopathic inferior, paranoid reaction types and paranoia, traumatic reactions, psychoneurosis, psychosomatic medicine and pathologic drinking. The problems of childhood make up the last chapter. The authors are justified in stating that the basic idea of psychosomatic medicine is ancient. Their plea for training of all medical students in psychiatry from the first day of entrance to school should be followed. The chapter on pathologic drinking is excellent. This book is highly recommended to all medical students and practitioners of medicine.

A Synopsis of Surgical Anatomy. By Alexander Lee McGregor, M.Ch., F.R.C.S., Surgeon, Johannesburg General Hospital, Johannesburg, South Africa. With a foreword by Sir Harold J. Stiles, K.B.E., F.R.C.S. Sixth edition. Cloth. Price, $6.50. Pp. 714, with 699 illustrations by Dr. E. A. Thomas. William Wood & Co., Mt. Royal & Guilford Aves., Baltimore 2; John Wright & Sons, Ltd., 28 Orchard St., Bristol 1, England, 1946.

This is always a valuable book, presenting in schematic and outline form a complete picture of human anatomy. The previous edition appeared in 1943, and thus only minor changes are to be expected. These revisions are chiefly apparent in the increased attention to the autonomic nervous system, the relative importance of which has increased in clinical significance. As always, this work can be recommended to those seeking a concisely diagrammatic review of anatomy.

Hobday's Surgical Diseases of the Dog and Cat. Edited by James McCunn, M.R.C.V.S., M.R.C.S., L.R.C.P., Professor of Veterinary Anatomy, Royal Veterinary College, London. Fifth edition. Cloth. Price, $6. Pp. 422, with 331 illustrations. William Wood & Co., Mt. Royal & Guilford Aves., Baltimore 2, 1947.

The first edition of this standard work appeared in 1900. This new edition does not differ greatly from the earlier ones. It is a manual which lists the commonest diseases of the dog and cat which require surgical care. Diagnostic procedures are not given much attention. The descriptions of surgical technics are adequate but somewhat outmoded in some instances. The book would be of some value to those who care for animal colonies used for medical research.

Essentials of Endocrinology. By Arthur Grollman, Ph.D., M.D., F.A.C.P., Professor of Medicine and Chairman of the Department of Experimental Medicine, the Southwestern Medical College, Dallas, Texas. Second edition. Fabrikoid. Price, $10. Pp. 644, with 132 illustrations. J. B. Lippincott Co., 227 S. Sixth St., Philadelphia 5, 1947.

The author has made several previous contributions to the literature on endocrinology. There is first a brief basic survey covering the scope and history of endocrinology and the origin, nature and uses of hormones. Thereafter, the subject is dealt with under five headings:

1. Endocrine glands of the cranial cavity (hypophysis, hypothalamus, pineal).
2. The branchiogenic organs (thyroid, parathyroid, thymus).
3. The endocrine organs of the abdominal cavity (pancreas, adrenals).
4. The hormones of the reproductive system (male, female).
5. The hormones derived from nonendocrine organs.

Under each gland there is a description of the anatomy, physiology, pathology and biochemistry, also a section on clinical considerations. Some clinical sections are good, but this is the minor part of the book. Since the book was written for the general practitioner, it seems overweighted in favor of descriptions of biologic and chemical investigations. Especially is this true of the section on the hormones of the reproductive system. Although the thymus and pineal have no known endocrine function at present, they are discussed at considerable length. There are tables giving commercially available endocrine products and their standardization.

The Guarantee of Annual Wages. By A. D. H. Kaplan. Cloth. Price, $3.50. Pp. 269. The Brookings Institution, 722 Jackson Place, N. W., Washington 6, 1947.

The Brookings Institution offers here a consideration of a proposal to improve the lot of persons who work for wages; emotional erosion may be the result of workers' fear of losing their jobs. However, a measure which meets the needs of one group may injure the interests of other groups. The author explains that guaranteed annual wages are suitable for certain industries—chiefly those with predictable seasonal variation in productivity. But to force all industries into the mold would require something akin to guaranteed production plans for each industry if member firms are to stay afloat. The minimum result would be the creation of new rigidities in a price system which works best when kept flexible and new monopolistic elements in an economy that works best without dominant agencies. The maximum result would be an approach to a fully planned industrial production. With either result, consumers would be offered only the products of firms which achieved mass production without much fluctuation in output. New enterprises, particularly new products, would become conspicuous by their absence.

The author's justifiable conclusion is that guaranteed annual wages have a place in the scheme of things, but that the nation's industry should not be dosed with a medicine that works for a specialized few of its member firms.

Pharmaceutical Laboratory Manual. By R. A. Kuever, Ph.G., Ph.C., Dean of the College of Pharmacy, State University of Iowa, Iowa City. Cloth. Price, $2.75. Pp. 290. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1947.

This compilation of one hundred and forty experiments in pharmaceutic compounding is intended for teaching pharmacy students. The experiments cover a wide range of preparations found in U. S. P. XIII and N. F. VIII, graded from the simple preparation of "waters," "solutions" and "infusions" to more complex preparations such as "vanishing cream" and "tooth paste." Many of the preparations are probably outmoded when viewed in the light of modern therapy. Each experiment leads to the production of a practical quantity of material, although the student may never later be called on to make such products. Directions for preparation and information concerning the uses and mode of administration, storage, constituents and the chemistry involved are provided for each product. A facing page of pertinent questions, with space for written answers, accompanies each experiment outline. The book contains much useful information for those pharmacy students whose interest may lie in the field of pharmaceutic manufacturing.

Lezioni di clinica medica [Vol. I°]. Di Luigi Condorelli, direttore della r. Clinica medica di Catania, Catania. Collana di scienze mediche, I. Boards. Price, 655 lire. Pp. 189, with 25 illustrations. Casa editrice A. P. E. (Azienda poligrafica editoriale), Corso Italia, 23, Catania, 1946.

Eight lectures delivered by Dr. Condorelli to his students make the content of the book. The cases chosen for discussion are of some interest, but some daring diagnoses such as that of pulmonic stenosis and patency of the ductus and that of coarctation of the aorta and patency of the ductus leave the reader perplexed on their exactness, in the absence of surgical or postmortem control and of more complete clinical work-up. The writing is redundant and verbose, and the frequent digressions from the case into entirely unrelated subjects make the presentation of material rather confused. The editorial form is commendable.

Surgical Pathology. By William Boyd, M.D., M.R.C.P., F.R.C.P., Professor of Pathology, The University of Toronto. Sixth edition. Cloth. Price, $12. Pp. 858, with 330 illustrations. W. B. Saunders Co., West Washington Square, Philadelphia 5, 1947.

It is interesting to compare this edition with the one of ten years ago. The space devoted to infections is now considerably smaller, as visible tribute to the effectiveness of the antibiotics. The chapter on shock has likewise shrunk, plasma and the blood bank having diminished the pathologists' supply of material from these sources. Thus the pathologist quickly reflects the trends of modern surgery. Congenital cardiac deformities, inaccessible lesions and obscure tumors of that era all are now within the surgeon's domain. The revisions made in this volume are needed to keep pace with the giant strides of modern medicine. It is heartening to see so many changes where least expected. The author has managed, as usual, to keep abreast of the tide and is maintaining the eminent place in pathology he long since attained.

Synopsis of Operative Surgery. By H. E. Mobley, M.D., F.A.C.S., Chief of Surgery at St. Anthony's Hospital, Morrilton, Ark. Second edition. Fabrikoid. Price, $6. Pp. 416, with 383 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1947.

Because this book contains "acute appendicitis is usually best handled by packing with ice, keeping the patient quiet and at rest for a few days until the acute inflamed condition subsides" it is not worth reviewing for scientific purposes.

Hospital and Public Health Resources in New Jersey: A Source Book. Part 1 of Report of New Jersey Survey of Hospital and Health Center Facilities under Federal Hospital Survey and Construction Act. Paper. Pp. 114, with illustrations. State of New Jersey, Department of Institutions and Agencies, Trenton, 1947.

Congress passed the Federal Hospital Survey and Construction Act to assist the several states in taking inventory of their existing hospitals, in surveying the need for construction of more hospitals and in developing programs for public and nonprofit hospitals. When completed, in combination with the present facilities, these programs should meet the need of adequate physical facilities capable of furnishing adequate services to all their inhabitants. The final step in this program is to construct the hospitals found to be needed.

In New Jersey (the state described in this pamphlet) the Department of Institutions and Agencies was assigned the task of administering the federal program. It is the duty of this department to present a plan showing the over-all need for additional hospitals and public health centers in the state. As this plan is being evolved, the department has issued this pamphlet as a source book. It contains information about all types of facilities for medical care available in New Jersey. This study presents a precise and complete view of the type and extent of services by hospitals, physicians, dentists, nurses, pharmacists and public health services in the state.

In regard to the general problem of meeting mounting hospital deficits and securing adequate reimbursement by the hospitals for the care of the indigent patient, the following is taken from a study recently made by the New Jersey Hospital Association and the New Jersey Department of Institutions and Agencies: "Only through governmental payments can the hospitals continue to furnish the service on which communities have come increasingly to depend as a central feature of the total health and welfare program."

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SECONDARY ANEMIA IN THE AGED

To the Editor:—Is folic acid indicated and has it any beneficial effect in the treatment of secondary anemia in a patient with advanced arteriosclerosis who is 82 years of age? Are there toxic side reactions?

Captain, M.C., U. S. Army.

ANSWER.—No reason exists for anticipating toxic manifestations from the moderate administration of folic acid to persons at any age. Though it is impossible to be certain that folic acid will be helpful to the patient cited in the query because of lack of precise information, it is highly probable that it will be helpful. Parenteral liver extract is more promising, however. In older persons one observes mixed forms of disorders more frequently than pure types. Diagnosis of specific disease entities in the elderly can be carried too far. For example, anemia is frequently due to both a nutritional (raw material) deficiency and a primary hemopoietic inadequacy. Unless both conditions are treated therapy is only partially successful. Similarly, many instances of chronic hypertrophic arthritis in later years are complicated by superimposed gout which is seldom discovered. Anemia even of minor degree in a patient aged 82 with advanced arteriosclerosis is a serious handicap: with loss of vascular flexibility the quality of the circulating blood becomes increasingly significant. Small (250 cc.) transfusions of blood followed by antianemic therapy are frequently helpful.

DIET IN TUBERCULOSIS

To the Editor:—In obese patients with pulmonary tuberculosis treated by rest in bed can weight be reduced to near normal without danger? What should be the composition of the diet, and how many calories per day, or per pound per day, should be allowed? The patient is 30 years of age, 6 feet 1 inch (185.42 cm.) tall and weighs 235 pounds (106.6 Kg.). How fast can the weight be reduced, and what should final weight be? Are high protein diets and high vitamin A diets as well as diets high in calcium and phosphorus of any therapeutic value in pulmonary tuberculosis?

M.D., Michigan.

ANSWER.—The main object in the dietetic treatment of the tuberculous patient is to enable him to regain his lost weight but not to make him unnecessarily fat. The weight of an obese, tuberculous patient can be safely reduced at the rate of 3 to 4 pounds (1.4 to 1.8 Kg.) per month, and his ideal weight is about 10 pounds (4.5 Kg.) above the average weight for his age and height. A reduction diet must include an increased supply of vitamin A and ascorbic acid to preserve nutritive equilibrium. Protein requirement is estimated at 1.5 to 1.75 Gm. per kilogram of body weight (Fishberg, M.: Pulmonary Tuberculosis, ed. 4, Philadelphia, Lea & Febiger, 1932, vol. 2), and carbohydrates should furnish about 40 per cent of the caloric requirements. The healthy person at complete rest requires 15 calories per pound (Goldberg, B.: Clinical Tuberculosis, ed. 5, Philadelphia, F. A. Davis Company, 1946, vol. 1) and from this standard a reduction diet can be estimated at the discretion of the physician. The patient's sense of well-being and satisfaction are factors to be considered. Thyroid extracts and amphetamine compounds are contraindicated. Diets rich in minerals have no proved value in the treatment of tuberculosis.

FLUOROSCOPY OF INFANTS

To the Editor:—Some pediatricians fluoroscope the infant at every monthly visit. What are the indications for fluoroscoping a child during the first year of life?

M.D., New York.

ANSWER.—It is generally considered good pediatric practice to fluoroscope an infant at the first office visit, usually when the child is 1 month of age. A few good pediatricians do not use a fluoroscope at all, except in the case of a sick infant. If no abnormalities are observed at the first fluoroscopic examination, it is unnecessary to refluoroscope the infant for a year or two, unless an illness develops that requires fluoroscopic aid in diagnosis. If at the first fluoroscopic examination an abnormality is observed such as a wide mediastinal shadow, enlarged heart or abnormal epiphysial development then progress might be observed every few months using the fluoroscope. Fluoroscopy of a well baby every month is bad practice because of the danger of repeated exposure to roentgen rays with their harmful effects.

AMENORRHEA

To the Editor:—A white woman aged 24 last had a regular menstrual period seventeen months ago. She started to menstruate at 13 years of age. The interval, duration and absence of cramps were all perfectly normal. Seventeen months ago the interval went from twenty-eight days to two or three months on two or three occasions, and then she stopped flowing. Her husband was overseas. The physical examination revealed a corpus which was slightly smaller than normal. Her basal metabolic rate was found to be minus 21 per cent and her red blood cell count was 4,100,000.

Therapy has consisted of an iron preparation, which has corrected her anemia, and thyroid which has brought her basal metabolic rate up to plus 1 per cent. She has been given three courses of "gonadogen" (a gonad-stimulating substance from serum of pregnant mares) in an attempt to establish a normal cycle. A day was assumed to be the first of a cycle and 10 units were given subcutaneously for fourteen consecutive days; in the event that she began to flow on or about the twenty-eighth day, the drug then would have been given similarly for fourteen more days. She did not flow spontaneously, so on the thirty-fifth day after the first dose of the first course of gonadotropic therapy the second fourteen day course was given. Daily 0.05 Gm. of ethinyl estradiol was taken by mouth for fourteen days concurrently with the gonad-stimulating substance. Then on the fifteenth, sixteenth and seventeenth days 10 units of progesterone was given parenterally. Three days after the last dose of progesterone she had a normal flow, the first in sixteen months. The record of daily basal temperatures before arising each morning has revealed that ovulation is not taking place, so this flow was probably on the basis of deprivation of progesterone in the presence of the estrogenic substance which had been taken by mouth.

Are any other measures suggested? She has not ovulated this third cycle. Ten units of the gonadotropic substance were given daily with the first day of flow, and then it was continued for fourteen days; no estrogen or progesterone has been given this time because, inasmuch as she is not ovulating, any flow would simply be based on deprivation of progesterone and not on ovulation.

M.D., California.

ANSWER.—As the amenorrhea in this patient is approximately of a year and a half's duration, it appears that there is some organic disturbance of the ovaries, since functional amenorrhea seldom lasts this long. Endometrial biopsies or even vaginal smears would be useful in indicating the degree of ovarian function. The refractoriness of the ovaries to gonadotropic therapy is confirmatory of the idea that the ovaries are damaged although gonadotropic therapy is at present on a rather unsatisfactory basis. Substitution therapy with ovarian hormones, estrogen and progesterone could probably cause a menstrual flow simulating the true cyclic bleeding when properly administered, but this does not relieve the basic condition. The suggestion is made that if it is possible a pelvic peritoneogram be made to demonstrate the size of the ovaries. Atropic ovaries would indicate the possibility of an irreversible condition. If the ovaries are normal in size or even moderately enlarged, it is possible that they are encased in a fibrous capsule which suppresses the cyclic activity of the ovaries. Such a condition often responds to partial resection of the ovaries with normal menstruation.

PHANTOM LIMB

To the Editor:—I have a patient who had a midthigh amputation eighteen months ago. He complains of moderate pain in the stump and of phantom limb. He has an artificial limb which he does not wear much. I have injected procaine hydrochloride and "trithesia (oil solution)" (propyl para-aminobenzoate 4 per cent; procaine base 1.5 per cent, and benzyl alcohol 5 per cent) a few times with only short relief. He resorts to alcohol or opiate at times for temporary relief. Please advise treatment.

G. C. Chamness, M.D., Zeigler, Ill.

ANSWER.—There is no conservative treatment for your case that will permanently relieve your patient of pain. If the latter is severe enough to cause him to take opiates and alcohol it is suggested that he have a competent neurosurgeon decorticate the area of the opposite postcentral gyrus receiving painful sensations from the involved thigh. This should produce complete loss of pain in the stump and in the phantom limb. This type of complication following amputations is not common. It is due, undoubtedly, to central processes which have no organic foundation in the central nervous system but in the peripheral nervous system. After the amputation there is irritation of the central conducting axons within a neuroma or at the proximal end of a freshly cut mixed nerve. These are the axons that formerly brought impulses to the higher centers from the part which has been amputated. Even after this irritation is removed the abnormal reflexes previously provoked continue to cause the sensations and pain. Such complicating symptoms can be prevented by placing a nonabsorbable ligature tightly around the uninjured nerve trunk about 1 inch (2.54 cm.) above the amputation site at the time of the amputation. An excellent article on the subject by Louis G. Herrmann and Edward W. Gibbs appeared in the *American Journal of Surgery* (47:168 [Feb.] 1940).

CONGENITAL MEGACOLON

To the Editor:—A boy aged 5 years was operated on for megacolon about six months ago because medical treatment was inadequate. The entire colon down to the rectosigmoid junction was removed and an ileocolostomy established using a Rankin clamp. The Rankin clamp was later removed and a fecal fistula was established. The patient had an enormous dilatation of his entire descending colon and about one-half of his transverse colon. Following the colectomy he was bothered considerably with distention. Discharges from the ileostomy were liquid in character. Distention was finally brought under control by the use of prostigmine. After thirty days the ileocolostomy was closed, supposedly in a satisfactory manner, but it reopened and was closed a second time. After the second closure the patient had bowel movements, liquid in character, and he again became distended. This condition was relieved by administration of prostigmine intramuscularly and orally. However, his ileocolostomy again broke down, and at present he has a small opening through which a great deal of fecal matter drains. At times he has a fairly normal bowel movement. His distention has gradually subsided, but his bowel movements continue to be soft and liquid. He has received prostigmine up until the last month and has gradually gained weight. He eats almost anything and feels well. I will close the opening of the ileocolostomy some time in the near future. Why do his bowel movements continue to be liquid and why has he had such an enormous amount of dilatation? Modifying his diet and using various preparations, including opiates, have had no effect on his stool. There is no reason to suspect an obstruction at the juncture of the ileum and rectum.

M.D., North Dakota.

ANSWER.—In congenital idiopathic megacolon there is, in addition to dilatation and hypertrophy of the bowel, a contraction of the rectosigmoid sphincter, the sphincter O'Beirne, and it is possible that the remaining distention in this instance and the reason for the breakdown of the ileocolostomy is because of the relative obstruction produced at this point. It is suggested that forceful dilation of the anal and rectosigmoidal sphincters be performed. This will probably permit the satisfactory closure of the fistula and will overcome the distention. The diarrhea is likely to persist for some time, because after a total colectomy the ileum does not take over the function of the large bowel. For this reason it would probably have been better not to have removed the entire colon but to have left a portion of the ascending colon at the time of the original operation. It is possible that the remaining portion of the rectosigmoid may take over the function of the colon sufficiently to permit the child to get along fairly well without too many bowel evacuations.

BILINGUAL CHILDREN

To the Editor:—I have been asked to solve the following problem: Should a couple of foreign birth (German) who speak their native language and English equally well try to teach their child, 1 year of age, both languages at the same time or teach him the foreign language later at the age of 5 or 6? As there seems to be some doubt as to the ability of the average child to learn two languages, would not an attempt at this lead to (1) retardation of development of speech in both languages; (2) due to the two languages having many similarities, the development of a mixture which may be hard to correct later, or (3) due to the inability to express himself according to his age, emotional maladjustment or even retardation of mental development?

M.D., Illinois.

ANSWER.—Prevailing opinion is that the child should be taught the single language, English, during its first five years. While many children can, and do, become bilingual in their early years without difficulty, there is a chance that any particular child might develop neurotic tendencies because of the bilingual pressure. In answer to the specific questions: (1) the average child (one with average intellectual ability and average auditory discrimination) might very well show a retardation or withdrawal from language due to the dual pressure; (2) a mixture of the two languages might occur if the pressure for perfection was severe in the home, leading to a relaxation away from the home, and (3) emotional maladjustment might well follow the conflict established in the child's mind by the dual language pressure, though it is questionable whether there would be mental retardation due to the attempt.

DISTILLED DRINKING WATER

To the Editor:—We are attempting to obtain information on the effects on infants and children of drinking distilled water over extended periods of time. Please supply reports or information on this subject.

J. P. Holt, M.D., New York.

ANSWER.—As long as an infant is ingesting milk, either human milk or customary formulas of cow's milk, and is retaining it, the intake of mineral salts will be ample with some to spare, so that he does not have to depend on the mineral content of the water consumed. Consequently distilled water would have no influence for good or evil. In an older child the absence of iodine and fluoride from distilled water might conceivably influence the development of goiter or dental caries. The fluorine ingested in foods is utilized much less than that in water. Distilled water per se would have no unfavorable influence provided the child were otherwise on a normal well balanced diet.

STREPTOMYCIN IN TUBERCULOSIS

To the Editor:—I am treating 7 patients with progressive pulmonary tuberculosis with streptomycin. Each has extrapulmonary tuberculosis; 2 have involvement of the spine and cold abscess formation. The others have either tuberculous laryngitis or a tuberculous fistula in ano. Treatment was discontinued in 2 patients because of dermatitis, headache and decided elevation of temperature. Vestibular disturbance occurred in all patients but was serious only in 1. Hypochromic macrocytic anemia has developed in all cases. The red blood cell count is 4,000,000 to 5,000,000 in all cases. Sahli hemoglobin determination is 70 to 45 per cent. Liver extract (10 units biweekly), liver and iron, ferrous sulfate alone, and folic acid have not helped. Is the hemoglobin reduction permanent? What therapeutic measures are indicated? Streptomycin sulfate was used in all cases. Is the hydrochloride better? The treatment period was one to four months. Results in those receiving 1.5 to 2 Gm. a day for two months have been dramatic. Is there a technic for desensitization of patients that have dermatitis?

M.D., Hawaii.

ANSWER.—G. L. Muller (Clinical Significance of the Blood in Tuberculosis, New York, the Commonwealth Fund, 1943. p. 215, 217) found an anemia (hemoglobin below 12 Gm. per hundred cubic centimeters) in 22 per cent of 1,130 patients with tuberculosis. Of those with anemia, 8.4 per cent had a macrocytic hypochromic type. A generalized intoxication is probably the most important etiologic factor. Indirect evidence for this is offered in the query by the failure of the patients to respond to liver, folic acid or iron therapy. If these patients have a megaloblastic bone marrow, folic acid and oral aqueous liver extract should receive further trial. The hemoglobin level should increase with improvement in the infection.

A recent report by the Veterans Administration, the Army and the Navy (The Effect of Streptomycin on Tuberculosis in Man, Preliminary Statement, *J.A.M.A.* **135**:634 [Nov. 8] 1947) and another by Farrington and co-workers (Farrington, R. F.; Hull-Smith, H.; Bunn, P. A., and McDermott, W.: Streptomycin Toxicity: Reactions to Highly Purified Drug on Long-Continued Administration to Human Subjects, *ibid.* **134**:679 [June 21] 1947) indicate that anemia is not a toxic manifestation of streptomycin therapy. The latter authors point out that identical toxic symptoms occur with streptomycin hydrochloride as with the sulfate.

No report was found of a technic for desensitizing patients to streptomycin. The pruritus associated with dermatitis is usually relieved by diphenhydramine hydrochloride ("benadryl hydrochloride"). Administration of streptomycin should be discontinued if exfoliative dermatitis occurs.

STREPTOMYCIN USED INTRAPERITONEALLY

To the Editor:—Is it advisable to put a solution of streptomycin in the peritoneal space around the cecum after removing an appendix covered with exudate or a perforated appendix?

John P. Gifford, M.D., Vero Beach, Fla.

ANSWER.—It is permissible to use streptomycin locally in the peritoneal space around the cecum after removing an appendix covered with exudate or a perforated appendix. It would be better, however, to inject streptomycin intramuscularly in amounts of 1 Gm. daily in divided doses every twelve hours for at least ten days when localized peritonitis is present. Parenteral therapy is always preferable to local treatment, and it is commonly more effective.

CYANIDE POISONING

To the Editor:—I read with interest your reply to the inquiry on cyanide poisoning in *The Journal*, Nov. 29, 1947, page 878. An error appears with regard to the chemistry of calcium cyanide. Calcium cyanide in the presence of moisture hydrolyzes rather rapidly, liberating hydrogen cyanide or hydrocyanic acid. This compound is not a skin irritant, although it may be absorbed through the skin. Cyanogen is not liberated from calcium cyanide on exposure to the moisture of the air. Cyanogen may be obtained from certain of the cyanides with difficulty, for example, on heating mercuric cyanide. Also, the reaction of potassium cyanide with copper sulfate yields cyanogen. Likewise, the dehydration of ammonium oxalate by means of phosphorus pentoxide liberates this compound.

Certain plants manufacture large quantities of hydrocyanic acid and its salts. Inevitably, a few accidents occur each year which result in acute hydrocyanic acid poisoning. Some of these cases have been rather severe, but in each instance the condition has responded more or less rapidly to the treatment suggested by Chen and his co-workers, i. e., the inhalation of amyl nitrite with artificial respiration, followed by the intravenous administration of sodium nitrite and sodium thiosulfate. In some cases unconsciousness has lasted for as long as eight hours. These cases, therefore, have given plant physicians an opportunity for accurate clinical observations. It is their considered opinion that such poisoning is an "all or none" type—that is, the patient either dies or recovers completely with no demonstrable residual pathologic condition.

They also believe that chronic cyanide poisoning does not exist, since small quantities of cyanide are detoxified so rapidly and completely, the cyanide apparently being converted to thiocyanates.

D. O. Hamblin, M.D., 30 Rockefeller Plaza, New York 20